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THE EFFECT OF THE NATURE OF THE GASEOUS MEDIUM UPON THE EVAPORATING RATE OF ALKALI CHLORIDES

Vikt. I. Spitsyn and V. I. Shostak

There are several references in the literature to the increased volatility of some inorganic substances when steam is present. It has been known for a long time that boric acid evaporates when heated in a current of steam, as well as when its aqueous solutions are distilled [1]. Silica can be evaporated when acted upon by steam at high temperature (1200-1300°) [2]. The present authors have shown [3] that normal sulfates of the alkali elements can be evaporated much more rapidly in a current of steam at 1200° than in a current of air. Spitsyn, Shostak, and Meerov [4] have found that alkali chlorides behave similarly, beginning at temperatures close to their melting points. The mechanism involved in these phenomena has not received a satisfactory explanation as yet.

The present research involved a study of the effect of the nature of the gaseous medium upon the evaporating rate of alkali chlorides. We chose the latter as our research objects because their chemical properties allowed of their being heated in various gaseous substances (air, steam, CO_2, HCl, NH_3) without reacting with them. The volatility of the alkali chlorides is perceptible even at comparatively low temperatures, which makes it easier to carry out the experiment.

The research procedure was as follows: a sample of the chloride (of the order of 0.25 g) was placed in a platinum boat. The latter was placed in another platinum boat of larger size in order to prevent loss of the molten salt by spattering against the walls. Heating was done in an electric furnace with an operating porcelain tube 20 mm in inside diameter. Temperature was measured with a platinum–platinum-rhodium thermocouple, one junction of which was located in the furnace, outside the operating tube, alongside the spot when the boats were placed. As a rule the tests were run at a temperature of 800°. The chlorides of all the alkali elements were tested. After their preparations had been fused they were analyzed for their chlorine content, the results proving to be quite satisfactory (Table 1).

TABLE 1
ANALYSIS OF CHLORIDES OF THE ALKALI ELEMENTS

Compound	Per cent chlorine	
	Experimental	Calculated
LiCl	83.59	83.63
NaCl	61.22	61.41
KCl	47.34	47.56
RbCl	29.38	29.32
CsCl	20.97	21.06

The alkali chlorides were calcined in currents of air, steam, and ammonia, the cesium chloride also being calcined in currents of hydrogen chloride and carbon dioxide. Before the air entered the operating tube, it was dried by passing it through bottles containing sulfuric acid and columns filled with phosphoric anhydride. The rate of evaporation of the alkali chlorides in a current of steam was investigated as follows. About 40 g of water was gently boiled in a small 50-ml Erlenmeyer flask. The steam generated flowed from the flask to the operating tube through a bent quartz connecting tube, tightly connected at either end by rubber stoppers. The end of the quartz tube projected far into the operating tube, being located in the hot zone at the beginning of the furnace, which prevented any partial condensation of the steam, the formation of drops, and the resultant cracking of the porcelain tube.

Graduations were marked on the flask to enable us to follow the rate at which the water was evaporated. The flask containing the water was weighed before and after the run to secure an accurate check. After a little practice it is easy to regulate heating so as to attain the desired rate of evaporation of the water: 18 grams per hour, as a rule. Reduced to standard conditions, this is equivalent to 0.37 liter per minute of water vapor. An Erlenmeyer flask with a capacity of about 100 ml, fitted with a reflux condenser served as the collector for the steam and the condensate. In the tests using ammonia, this latter gas was produced by heating a commercial

aqueous solution, and it was dried by passing it through columns filled with pieces of sodium hydroxide and lime. The ammonia was drawn through the operating tube containing the boat with the test substance at the required rate by means of a water-jet pump. The carbon dioxide was taken from a tank. It was first dried with sulfuric acid and phosphoric anhydride. The hydrogen chloride was prepared by reacting sodium chloride with concentrated sulfuric acid. It was dried in the same manner as the air and the carbon dioxide. The rates of flow of the air, ammonia, carbon dioxide, and hydrogen chloride were checked by means of rheometers.

Tables 2, 3, and 4 give the results of our calcination of alkali chlorides in currents of air, steam, and ammonia. The quantity of gas passing through was kept as approximately 0.4 liter/minute (at standard conditions).

TABLE 2

EVAPORATION OF CHLORIDES OF THE ALKALI ELEMENTS IN A CURRENT OF AIR AT 800°

Air rate: 0.35-0.37 liter/minute. Calcining time: 30 min.

Chloride	Initial sample, grams	Loss of weight		
		Grams	Per cent	Millimoles
LiCl	0.2505	0.0274	10.94	0.65
NaCl	0.2497	0.0080	3.20	0.14
KCl	0.2451	0.0201	8.20	0.26
RbCl	0.2525	0.0296	12.00	0.25
CsCl	0.2515	0.0641	25.49	0.38

TABLE 3

EVAPORATION OF CHLORIDES OF THE ALKALI ELEMENTS IN A CURRENT OF STEAM AT A TEMPERATURE OF 800°

Calcination time: 30 min. Evaporation rate: 18 g/hour (0.37 liter/min).

Chloride	Test No.	Initial weight grams	Loss of weight			Mean (millimoles)
			Grams	Per cent	Millimoles	
LiCl	1	0.2540	0.0513	20.20	1.21	1.20
	2	0.2512	0.0507	20.18	1.19	
NaCl	3	0.2478	0.0106	4.28	0.18	0.18
	4	0.2489	0.0112	4.50	0.19	
KCl	5	0.2530	0.0245	9.69	0.32	0.33
	6	0.2515	0.0260	10.34	0.35	
RbCl	7	0.2504	0.0552	22.04	0.45	0.44
	8	0.2514	0.0522	22.76	0.43	
CsCl	9	0.2521	0.0870	34.51	0.52	0.52
	10	0.2505	0.0869	34.69	0.52	

Lithium and cesium chlorides, which have the lowest boiling points (1382 and 1303°, respectively), exhibit the maximum rate of evaporation in a current of air, and, obviously, at any one temperature they exhibit a higher vapor pressure than the chlorides of the other alkali elements. Sodium chloride, which has the highest melting point (800°) and boiling point (1465°) of all the alkali chlorides, exhibits the minimum rate of evaporation.

In a current of steam, the rate of evaporation of the chlorides of the alkali elements is much higher than when they are calcined in a current of air. This is particularly striking in the salts of lithium, rubidium, and cesium, whose molar evaporation rate rises 84.6%, 70% and 37% respectively, or by factors ranging from 1.8 to 1.4. The increase in the loss of weight is less in the other chlorides (Table 3). The evaporation rates of the various chlorides bear the same relationship to one another as in calcination in a current of steam.

The rate of evaporation of alkali chlorides may be increased substantially by increasing the rate of flow of the steam through the operating tube. The example of cesium chloride is used in Table 4 and Fig. 1 to show that nearly all the original sample can be evaporated during a given interval of time (30 min) when the steam flows at the rate of 180 g/hr, whereas evaporation is only approximately one-third complete when the rate is

18 g/hr. It should likewise be borne in mind that the observed loss of weight of the chloride does not proportionally to the increase in the rate of steam flow, but is somewhat different from the latter. A 200% increase in the rate of steam flow, for example, increases the chloride loss of weight only 50-100 %.

TABLE 4

EVAPORATION OF CESIUM CHLORIDE AT VARIOUS RATES OF STEAM FLOW

Temperature: 800°. Calcination time: 30 Min.

Test No.	Initial weight, grams	Rate of steam flow, g/hr	Loss of weight		
			Grams	Per cent	Millimoles
1	0.2521	18	0.0870	34.51	0.52
2	0.2502	36	0.1140	45.56	0.68
3	0.2478	54	0.1560	62.65	0.84
4	0.2532	180	0.2414	95.34	1.43

TABLE 5

EVAPORATION OF CHLORIDES OF THE ALKALI ELEMENTS AT 800° IN A CURRENT OF AMMONIA

Rate of ammonia flow: 0.35 liter/min. Calcination time: 30 min.

Chloride	Test No.	Initial weight, grams	Loss of weight			Mean (Millimoles)
			Grams	Per cent	Millimoles	
LiCl	1	0.2534	0.0457	18.03	1.07	1.08
	2	0.2517	0.0462	18.30	1.09	
NaCl	3	0.2487	0.0061	2.45	0.10	0.11
	4	0.2505	0.0077	3.07	0.13	
KCl	5	0.2508	0.0187	7.46	0.25	0.26
	6	0.2497	0.0202	8.09	0.27	
RbCl	7	0.2483	0.0488	19.65	0.40	0.39
	8	0.2491	0.0474	19.03	0.39	
CsCl	9	0.2496	0.0834	33.43	0.50	0.49
	10	0.2517	0.0820	32.58	0.49	

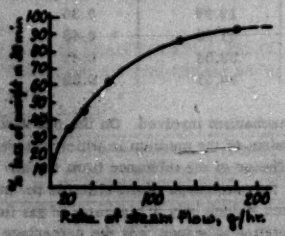

Fig. 1.
Effect of the rate of steam flow upon the evaporation of cesium chloride at 800°.

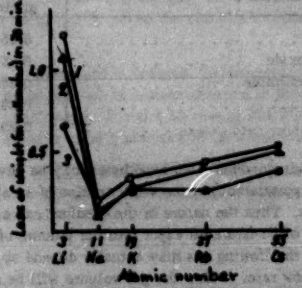

Fig. 2.
Rate of evaporation of chlorides of the alkali elements at 800° in various gaseous media.

1—In a current of steam; 2—In a current of ammonia; 3—In a current of air.

As Table 5 shows, the rate at which the alkali chlorides are evaporated in a current of ammonia follows the same pattern as exhibited in a current of air or of steam: the volatility decreases as we pass from the lithium salt to sodium chloride and increases in the other chlorides. Lithium and cesium chlorides exhibit the greatest loss of weight.

The evaporation rate of chlorides of the alkali elements in a current of ammonia is, in general higher than in a current of air. The singular behavior of sodium and potassium chlorides is worthy of note; they exhibit practically the same loss of weight in an air current as in an ammonia current. The evaporation rate of all the chlorides in ammonia is somewhat lower than their evaporation rate in a current of steam, however (about 5-14% less, and as much as 60% less for the sodium salt).

The molar evaporation rates of all the alkali chlorides in currents of air, steam, and ammonia are compared in Table 6 and Fig. 2.

TABLE 6

COMPARATIVE EVAPORATION RATES OF CHLORIDES OF THE ALKALI ELEMENTS IN CURRENTS OF AIR, AMMONIA AND STEAM

Temperature: 800°. Calcination Time: 30 Min. Average size of sample: 0.25 g

Chloride	Loss of weight, millimoles		
	In a current of air (0.35-0.37 liter/min)	In a current of ammonia (0.35 liter/min)	In a current of steam (0.37 liter/min)
LiCl	0.65	1.08	1.20
NaCl	0.14	0.11	0.18
KCl	0.26	0.26	0.33
RbCl	0.25	0.39	0.44
CsCl	0.38	0.49	0.52

We also investigated the effect of carbon dioxide and hydrogen chloride upon the rate of evaporation of cesium chloride at 800°.

The results of our tests of the evaporation of cesium chloride in various gaseous media are listed in Table 7.

The cesium chloride evaporates at about the same rate in hydrogen chloride as it does in ammonia, and somewhat more slowly in carbon dioxide than in hydrogen chloride. The gaseous media tested may be arranged as follows in order of increasing amounts of cesium chloride entrained by a given volume of gas: carbon dioxide, air, hydrogen chloride, ammonia, steam. This series becomes especially striking when when we compare the absolute quantities of cesium chloride passing over into a gaseous volume of 12 liters during 30 minutes. This is 0.0501 g for carbon dioxide and 0.0870 g for steam.

It was shown above that steam increases the evaporation of all the alkali chlorides to some extent, with ammonia increasing evaporation for most of them. It may be assumed that the effect of HCl and CO_2 atmosphere upon the volatility of the other alkali chlorides is about the same as we have observed in the case of cesium chloride. The variation of the evaporation rate of alkali chlorides with the nature of the gaseous medium is a highly

TABLE 7

EVAPORATION RATE OF CESIUM CHLORIDE IN VARIOUS GASEOUS MEDIA AT 800°

Rate of gas flow: approx. 0.4 liter/min. Calcination time: 30 min.

Medium	Initial weight, grams	Loss of weight		
		Grams	Per cent	Millimoles
Air	0.2562	0.0650	25.37	0.39
Carbon dioxide	0.2506	0.0501	19.99	0.30
Hydrogen chloride	0.2584	0.0816	31.58	0.48
Ammonia	0.2517	0.0820	32.58	0.49
Steam	0.2521	0.0870	34.51	0.52

singular phenomenon. Two hypotheses may be advanced concerning the mechanism involved. On the one hand, it may be postulated that the vapor tension of an alkali chloride is independent of the medium in which evaporation occurs. Then the nature of the medium can affect only the rate of diffusion of the substance from the surface layer of its saturated vapor into the volume of the flowing gas. Then the percentage of the chloride per unit volume of the flowing gas may actually depend upon the nature of the latter, though only at high rates of gas flow At rather low rates of flow the gas volume will be saturated with the evaporating substance, and the percentage of the chloride per unit volume of the flowing gas should be the same for various media.

On the other hand, we cannot dismiss the hypothesis that the vapor pressure of the chloride varies with the nature of the flowing gas, due to physicochemical interaction between the gas and the surface layer of the evaporating substance. Then saturation of the unit volume of gas with the chloride will result in the percentage of the chloride in the gas varying with the nature of the latter. To check these hypotheses we ran tests intended to achieve saturation when evaporating cesium chloride in currents of air and steam. The gas flow ranged from 1 liter/min to 0.05-0.10-liter/min. The experimental findings are listed in Tables 8 and 9.

TABLE 8

EVAPORATION OF CESIUM CHLORIDE AT VARIOUS RATES OF AIR FLOW

Temperature: 800°. Calcination time: 30 min.

Test No.	Initial weight, grams	Rate of gas flow (liters/min at standard conditions)	Loss of weight		Loss of weight per liter of gas, mg
			Grams	Per cent	
1	0.2539	1.00	0.0612	24.10	2.1
2	0.2552	0.40	0.0650	25.37	5.4
3	0.2546	0.30	0.0622	24.43	6.9
4	0.2482	0.20	0.0518	20.87	8.6
5	0.2512	0.15	0.0508	20.30	11.4
6	0.2508	0.10	0.0565	22.53	18.8
7	0.2550	0.05	0.0277	10.86	18.4

TABLE 9

EVAPORATION OF CESIUM CHLORIDE AT VARIOUS RATES OF STEAM FLOW

Temperature: 800°. Calcination time: 30 min.

Test No.	Initial weight, grams	Rate of gas flow (liters/min at standard conditions)	Loss of weight		Loss of weight per liter of gas, mg
			Grams	Per cent	
1	0.2478	1.12	0.1560	62.65	3.6
2	0.2502	0.74	0.1140	45.56	5.1
3	0.2521	0.37	0.0870	34.51	7.7
4	0.2509	0.18	0.0489	19.49	8.1
5	0.2433	0.15	0.0500	20.55	11.1
6	0.2547	0.10	0.0570	22.38	19.0

These tests definitely indicate that the maximum quantity of cesium chloride in 1 liter of gas passing at the rate of 0.1 liter/min above a sample of the preparation at 800° is practically the same in both of the media tested, being 18.8 mg for air and 19.0 mg for steam. Hence, at low rates of gas flow the amount of chloride evaporated equals the quantity escaping at "zero" velocity, no matter what the nature of the gas. Doubtless, in this case the gas is saturated with cesium chloride vapor, the saturation being equivalent to the chloride's vapor pressure at the given temperature.

TABLE 10

COMPARATIVE EVAPORATION RATES OF CESIUM CHLORIDE IN CURRENTS OF AIR AND STEAM AT VARIOUS RATES OF GAS FLOW

Temperature: 800°

Rate of gas flow, liters/min	Loss of weight of cesium chloride per liter of gas (at standard conditions)	
	In a current of air	In a current of steam
1	2.1	3.6
0.4	5.4	7.7
0.2	8.6	8.1
0.15	11.4	11.1
0.10	18.8	19.0
0.05	18.4	—

Flock and Rodebusch [5] investigated the vapor pressure of cesium chloride in the 824.7-1304° range. It was 4.15 mm at 824.7°; we found it to be 2 mm at 800° by extrapolation.

We calculated the partial pressure of cesium chloride at "zero" velocity of the gas from the formula:

$$p = \frac{n}{n + N} P,$$

where n is the moles of evaporated substance (based on 1 liter of gas), N is the moles of gas per liter (equaling 0.04464), and P is the total pressure in the system (760 mm).

Using the figures in Table 8 (for evaporation in a current of air) and in Table 9 (for steam) and taking the molecular weight as 168.37, we get the following values for the vapor pressure of cesium chloride at 800°.

a) 1.89 mm for air; b) 1.92 mm for steam.

These two values are practically the same as the extrapolated value for the vapor pressure of cesium chloride given above.

The quantities of cesium chloride in 1 liter of air and steam are listed in Table 10 and plotted in Fig. 3 for various gas velocities.

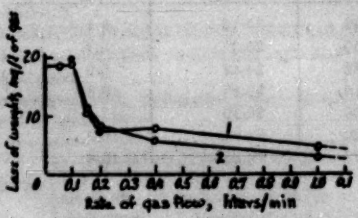

Fig. 3. Effect of the velocity of air and steam current upon the evaporation of cesium chloride at 800°.
1—Steam; 2—Air.

This comparison shows that steam speeds up the evaporation of cesium chloride more than air does at relatively high rates of gas flow (0.4-1 liter/min). But as we descend to 0.2 liter/min, the loss of weight of the cesium chloride begins to be the same in steam and in air, even though the gas is not yet saturated with cesium chloride vapor. All these tests make the following explanation of the influence of the nature of the gaseous medium upon the evaporation rate of the alkali chlorides most probable.

As we know, there is a layer of saturated vapor (the "diffusion layer") at the surface of an evaporating solid or liquid. There is no doubt that there is a force of attraction operating between the molecules that constitute the diffusion layer. The molecules of the passing gas mix with the chloride vapor at the boundary of the diffusion layer, surround the chloride molecules, and establish a singular envelope about the latter, weakening the bond between the chloride molecules and entraining them with the gas stream. The more sharply expressed the polar nature of the alkali chlorides, the more easily is this envelope established by the more highly polar gases.

As a matter of fact, if we arrange the polar substances we employed as gaseous media in our cesium chloride tests in order of increasing polarity, we find that their order agrees exactly with the rise in the influence of these substances upon the rate at which the chloride evaporates (see Table 7):

Substance	Dipole moment ($\mu \cdot 10^{18}$)
CO_2	0
Air (nitrogen, oxygen)	0
HCl	1.0
NH_3	1.4
H_2O	1.8

Thus, steam "erodes" the diffusion layer most, with air and carbon dioxide eroding least of all. It is obvious that the thickness of the diffusion layer will also vary, being thinnest in the case of steam and a maximum when the cesium chloride is evaporated in a current of air or carbon dioxide. The rate of diffusion of gaseous substances is high, in general, at elevated temperatures; hence, at low velocities of the passing gas, the evaporating substance is able to diffuse rapidly enough in any of the media we employed, saturating it.

When the rate of flow of the passing gas is such that it is not fully saturated with the chloride vapor, a greater degree of saturation will be found in the media that ensure the maximum rate of diffusion of the vapor into the volume of the passing gas. We used the data in Table 6 to compute the degree of saturation of various media with cesium chloride vapor at 800° and a gas velocity of 0.4 liter/min. (Table 11).

The minimum saturations (26.0 and 28.6%, respectively) were found for carbon dioxide and air. The saturation rises to 36% for hydrogen chloride and ammonia, attaining the highest value for steam (40.7%).

The explanation given above for the way in which the nature of the gaseous medium affects the evaporation rate of cesium chloride probably applies to other types of inorganic compounds as well as all the alkali chlorides.

TABLE 11

DEGREE OF SATURATION OF VARIOUS GASEOUS MEDIA WITH CESIUM CHLORIDE VAPOR

Temperature 800°. Rate of gas flow: 0.4 liter/min. Theoretical maximum content of cesium chloride in the passing gas: 18.9 mg/liter

Gaseous medium	Cesium chloride evaporated, mg per liter of gas	Per cent saturation of the gas with cesium chloride vapor
CO_2	4.9	26.0
Air	5.4	28.6
HCl	6.8	36.0
NH_3	6.8	36.0
Steam	7.7	40.7

SUMMARY

1. A study has been made of the rate at which the chlorides of all the alkali elements evaporate at 800° in currents of air, steam, and ammonia, and of the evaporation rate of cesium chloride in carbon dioxide and hydrogen chloride as well.

2. At a constant temperature (800°) and a constant rate of gas flow (of the order of 0.4 liter/min) lithium chloride exhibits the maximum rate of evaporation and sodium chloride the minimum. Sodium chloride is followed by potassium, rubidium, and cesium chlorides in order of increasing evaporation rate.

3. It has been established that when the rate of gas flow is high (0.4 liter/min and up), the greater the polarity of the medium in which heating is effected, the higher the rate of evaporation of the alkali chlorides.

4. The polarity of the gaseous medium has the least effect upon the evaporation of sodium chloride and the most effect upon lithium and cesium chlorides. The rate of evaporation of lithium chloride in a current of steam is nearly twice as great as in a current of air.

5. At low rates of gas flow (0.2 liter/min and below), the evaporation rates of the alkali chlorides become identical in various gaseous media.

6. It is suggested that the increased polarity of the gaseous medium facilitates the "erosion" of the diffusion layer at the surface of the evaporating substance. This may be due to the physicochemical interaction of the molecules of the passing gas with the molecules of the evaporating substance in the latter's diffusion layer.

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*See Consultants Bureau translation, p. a-251.

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THE VOLATILITY OF ALKALI CHLORIDES WHEN THEIR AQUEOUS SOLUTIONS ARE EVAPORATED

Vikt. I. Spitsyn and M. A. Meerov

In preceding reports [1] we have shown that alkali chlorides evaporate substantially in a current of steam at temperatures approaching their boiling points.

In 1894 Bailey [2] published his observations on the volatility of alkali element chlorides during the evaporation of their aqueous solutions. His qualitative experiments must be regarded as hardly convincing: a filter paper held just above the surface of a solution heated on a water bath exhibited the presence of a chloride after some time had passed, but this might have been caused by contamination from the air. Bailey's quantitative experiments were made by evaporating about 3 liters of solution of each alkali chloride, of approximately N/10 concentration, in 100-ml platinum beakers. Bailey found the loss to be greatest in the case of cesium chloride: 3.5 mg per liter of evaporated solution, and least in the case of lithium chloride: 0.25 mg/liter. The loss rose with an increase in the solution concentration; but even these results are open to doubt, inasmuch as the loss of chloride was determined indirectly, by analyzing a sample of the remaining solution for chloride by precipitation or by titrating it with silver nitrate. The losses found were 0.2% - 0.3% of the total chloride content in the initial solutions, which lies within the limits of error of the method of analysis employed.

The problem of the volatility of alkali chlorides when their aqueous solutions are evaporated in air is of practical as well as theoretical importance, as, for instance, in performing analyses for the rare alkali elements. That is why we subjected Bailey's observations, which are referred to in the literature, to a check and, as will be shown later on, failed to confirm them.

In our experiments 50 ml of decinormal solutions of the alkali chlorides were evaporated in platinum beakers on a water bath, the contents of the beakers being kept constant by gradually adding water. The quantity of water used totalled 3 liters. After the run was over, the solution was evaporated to dryness in the same beaker. The residue was heated to constant weight at 250°, the quantity of salt present thus being determined directly. At the same time we applied a correction for the nonvolatile residue contained in the distilled water used (0.0004 g/liter). The results of our tests are given in Table 1. None of the chlorides tested exhibited any loss of weight when its aqueous solution was evaporated. The slight gain in weight (of the order of 0.4-0.6 mg) over the initial value is probably due to the settling of a slight amount of air-borne dust into the solution. The latter cannot be ignored, notwithstanding the precautions taken, inasmuch as the tests lasted approximately 1 month.

TABLE 1

CHANGE IN WEIGHT OF CHLORIDES OF THE ALKALI ELEMENTS WHEN 3 LITERS OF WATER CONTAINING 0.005 GRAM EQUIVALENT OF THE SALT ARE EVAPORATED

Substance	Grams of salt	
	Before evaporation	After evaporation
LiCl	0.2130	0.2136
NaCl	0.2924	0.2928
KCl	0.3434	0.3738
RbCl	0.6050	0.6054
CsCl	0.8400	0.8404

We also investigated the boiling of solutions of cesium chloride of various concentrations, analyzing the distillate or the residue for cesium by the chloroplatinate method (Table 2). Here again we discovered absolutely no loss of the alkali chloride. Similar results were obtained when we boiled solutions of the chlorides of the other alkali elements.

SUMMARY

1. The behavior of alkali chlorides when their aqueous solutions are boiled in air has been investigated.

TABLE 2

CHANGE IN WEIGHT OF CESIUM CHLORIDE WHEN ITS AQUEOUS SOLUTIONS ARE BOILED

Test No.	Research method	CsCl used, grams	CsCl found, grams	
			In residual solution	In distillate
1	Boiling 100 ml of solution for 6 hours in a flask fitted with a condenser to collect the distillate (approximately 50 ml being collected)	1.0	Not determined	None
2	Boiling 100 ml of solution for 3 hours in an open beaker, the volume being maintained constant by adding water	0.1764	0.1768	–

2. It has been established that the alkali chlorides do not evaporated together with the steam. The findings set forth in the earlier paper by Bailey on this problem have not been confirmed.

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* See Consultants Bureau translation, p. 821.

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A METHOD OF PREPARING STABLE SOLUTIONS OF SODIUM AND POTASSIUM ZINCATES

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Solutions of zinc oxide in alkalies, known as zincate solutions, have recently begun to be employed in practice as an electrolyte for galvanic cells of the VDSP type and for the Drumm zinc-nickel storage battery [1] or as the major constituent of the electroplating baths proposed by Kudryavtsev and Nikiforova [2] and by Dexiderlev [3].

The growth in practical interest in solutions of this sort made a more thorough study of them necessary.

As we know, one of the characteristics of zincate solutions is their low stability with time. This phenomenon, known as "aging," manifests itself as follows: the zinc oxide dissolved in the alkali forms unstable solutions from the start, which contain an excess of zinc that settles out with time as zinc oxide or zinc hydroxide. We have as yet no satisfactory explanation for this phenomenon of "aging". As a rule, the reason for the differences in the percentage of zinc oxide in the solution is sought in the changes occurring in the bottom phases, little attention being paid to possible changes in the composition of the zincate molecules within the solution itself.

Many papers on the physicochemical investigation of zincate solutions have dealt with the problem of the solubility of zinc oxide in sodium hydroxide. There has been hardly any systematic research on the solubility of zinc oxide in potassium hydroxide.

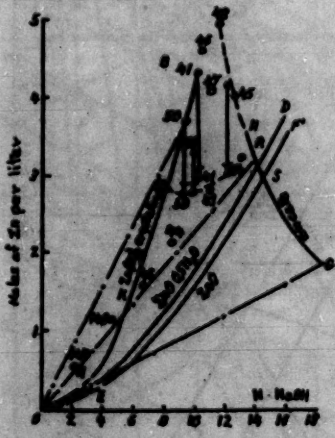


Fig. 1
Solubility isotherms of zinc oxide and hydroxide in NaOH.

To solve the applied-chemistry problem, involving the determination of the region within which zincate solutions are stable, we utilized the data in the literature for sodium zincate and ran experimental tests for the potassium zincates. The papers by Goudriaan [4, 8], Kaufmann [5, 8], Muller [6], and Scholder [7] are outstanding among those dealing with sodium zincates.

Muller's paper contains carefully collected experimental data on the solubility of zinc oxide and amorphous hydroxide [1] in sodium hydroxide solutions. Scholder's researches [7, 9] also describe the composition of solid sodium zincates and their solubility in alkali. Muller plotted the results of his research in a rectangular diagram (Fig. 1), with the alkali concentration laid off along the axis of abscissas and the equilibrium content of zinc oxide in molecules per liter along the axis of ordinates. The solid lines represent the solubility isotherms of one of the products used in sodium hydroxide solutions at 30°.

The system of rectangular coordinates chosen by Muller suffers from this disadvantage: this form

[1] Henceforth the term "amorphous hydroxide" is employed to differentiate from the clearly crystalline, as say, the rhombic hydroxide, although all forms of zinc hydroxide are of crystalline structure according to Hedval's X-ray analysis [Z. allg. anorg. Ch., 120, 327 (1922)].

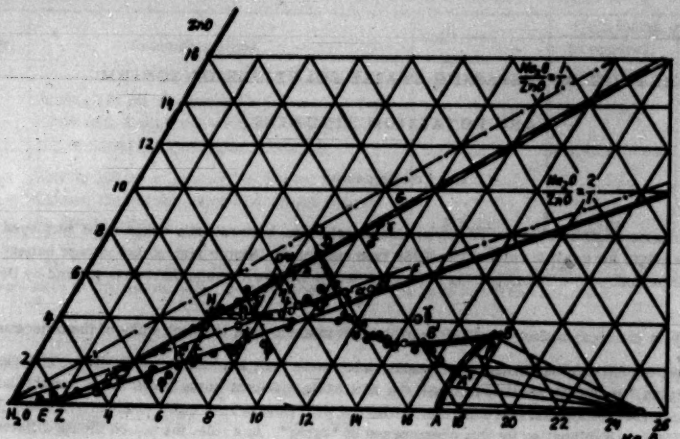


Fig. 2. Limits of stable and unstable equilibrium in solutions of sodium zincate.

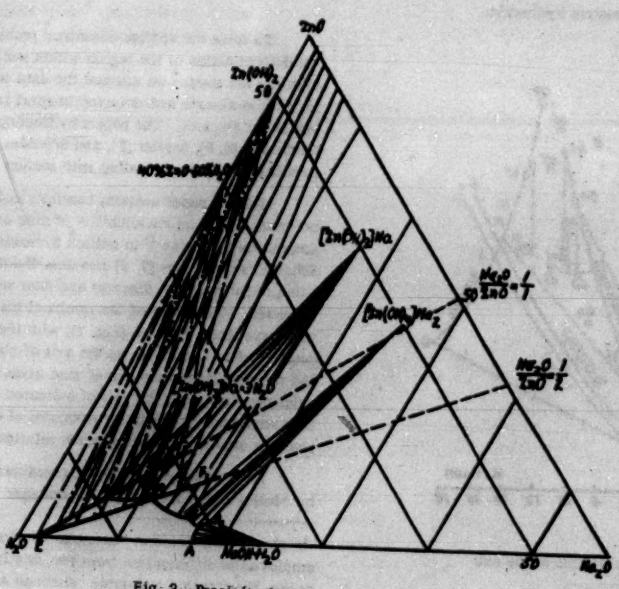
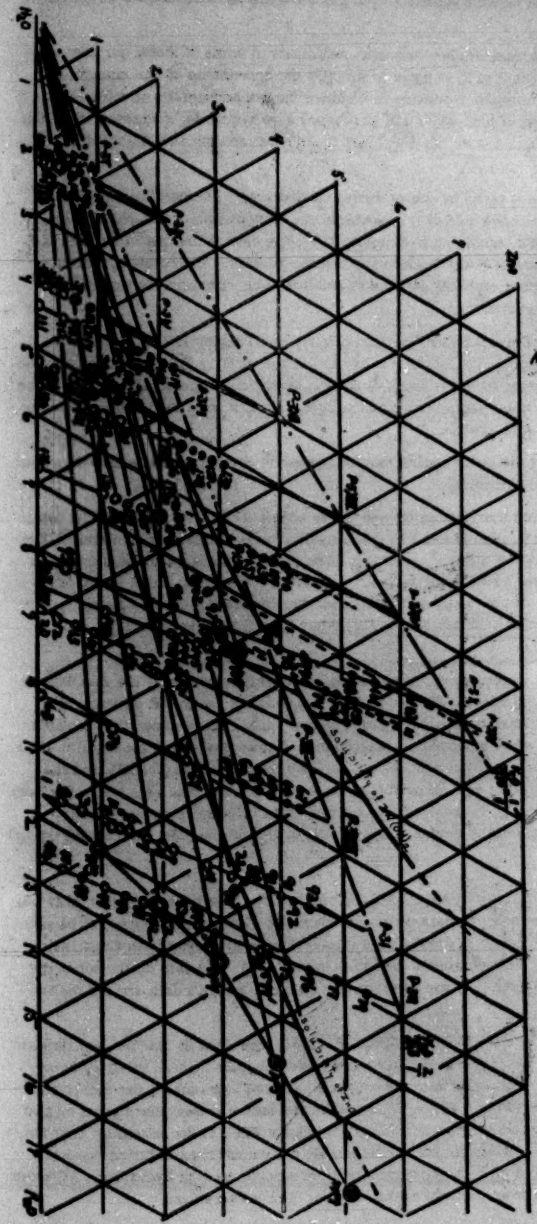


Fig. 3. Precipitation rays of a bottom phase.



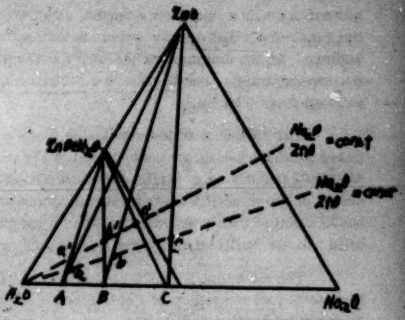


Fig. 5. Schematic representation of the solution of zinc oxides in an alkali.

Fig. 4. Solubility of zinc oxide and crystalline zinc hydroxide in KOH solutions at 18-20°.

of representation does not clearly show the change in the concentration of water, which is the third constituent in the $Na_2O-ZnO-H_2O$ system. The complication of the diagram when high-concentration solutions are employed is another disadvantage.

We have recalculated the data of Goudriaan, Muller, Scholder, and others in terms of molar per cent and plotted them in a triangular diagram, as shown in Fig. 2, in order to simplify the appearance of the equilibria in the $Na_2O-ZnO-H_2O$ ternary system as well as to make it possible to compare the research results of different authors. In this diagram the solubility isotherm of zinc oxide and amorphous zinc hydroxide is represented by the coinciding straight line EF, which exhibits a curve toward the 100% H_2O triangle vertex only in a highly dilute solution (over 97% H_2O).

The solubility of the crystalline zincate is given by the isotherms BD and B'A'. The equilibrium bottom phase within this diagram ought to lie on the concave side of this isotherm, the composition of this phase being $NaHZnO_2$ (according to Muller [6]) or $Zn(OH)_2Na$ (according to Scholder [7]). The dashed line AA' indicates the course of the solubility isotherm of the monohydrate $NaOH \cdot H_2O$ in the zincate solution. The Point A represents NaOH solution that is saturated at 30°, its composition being 54% NaOH and 46% H_2O. The composition of the solid hydrate $NaOH \cdot H_2O$ is given by the point at 25% Na_2O.

The isotherms EF, CB', B'A' and A'A in Figures 2 and 3 delimit a fairly small region EFB'A'A, which we propose to call the region of stable zincate solutions, i.e., solutions that do not age at 30°. These solutions may be prepared by dissolving the crystalline zincate, zinc oxide, or amorphous zinc hydroxide in the alkali. Any solution whose compositions is found to lie outside the stable region is subject to aging, since it may decompose with time, throwing down a precipitate and producing a stable solution.

The reproducibility of the boundaries of the stable region may be judged by comparing the results obtained by Müller with, say, the results of Goudriaan and Scholder.

Goudriaan's points are denoted in Figure 2 by solid circles and Greek letters α, β, γ, φ, ϑ, μ and η, while Scholder's points are denoted by half-filled circles and Müller's by circles with crosses inscribed within them. The satisfactory agreement of the results obtained by the different authors is direct proof of the stability of solution within the EFB'A region and, therefore, proof that equilibrium exists in this part of the system, which has been the subject of discussion between the adherents of the theory of pseudo solutions: Hantzsch [10] and Chatterji and Dhar [11], and the champions of the theory of true solutions: Bredig [12], Moir [13], Goudriaan, Scholder, and others.

When we plot the Müller points (circles with crosses), representing the solubility of crystalline $Zn(OH)_2$, in the diagram (Figure 2), we note that the points in the vicinity of 4 and 6% Na_2O do not lie on the isotherm EF, whereas the point 41, near 8% Na_2O, lies on the straight line. We find, however, as Müller remarks, that the composition corresponding to this curve is obtained when an abundant precipitate is thrown down from the solution after 13 days of standing. This is evidence of disturbance of the equilibrium between the crystalline $Zn(OH)_2$ and the alkali. If we plot the point representing a solution in equilibrium with the crystalline $Zn(OH)_2$, i.e., a solution from which no precipitate settles out as yet (see Point 41), in the diagram, we find that this point lies close to the straight line EG that passes through the points referred to (close to 4% and 6% Na_2O) and the point on the $ZnO-Na_2O$ side of the triangle where $\frac{Na_2O}{ZnO} = \frac{1}{1}$ (Figure 3).

The location of the solubility isotherm for crystalline $Zn(OH)_2$, plotted on the basis of three points, may be regarded as hardly convincing. But when we superpose the data of other authors, we find the coincidence to be satisfactory. Evidence of this is the position of the points μ and η [solid circles (Figure 2)], taken from Goudriaan's diagram and the half-filled circles plotted from the recomputed data of Scholder's [7]. The data on the solubility of rhombic $Zn(OH)_2$, specially investigated by Fricke [14], are of particular interest. Fricke's data are plotted in Figure 2 as circles with numbers alongside them.

The Fricke data (Points 4, 5, 6, and 7), like the Müller findings (Point 41), convince us that the equilibrium between crystalline $Zn(OH)_2$ and the solution is not stable at 30° in concentrated solutions. These solutions break down within a comparatively short time, throwing down an amorphous precipitate and approaching the composition corresponding to equilibrium solutions along the isotherm EF, as indicated by the dotted arrow. The figures on the solubility of crystalline $Zn(OH)_2$ enable us to demarcate part of still another region EDFE in the triangular diagram, which may be called the region of unstable, i.e., aging zincate solutions. We can secure these solutions by dissolving crystals of $Zn(OH)_2$ in an alkali in the cold or by heating zinc oxide or amorphous zinc hydroxide. All these solutions are unstable, precipitates being thrown down from them shortly after their preparation.

If the isotherm EG refers to a highly unstable state in concentrated solutions, the stability of the systems consisting of crystalline $Zn(OH)_2$—solution rises as dilution is increased.

The boundary at which the unstable system is transformed into a more highly stable one evidently lies close to Fricke's point 4 (the intersection of the isotherms GE and HC in Figure 2). This comparatively high stability of the equilibrium in the region extending from the point 4 to E explains the formation of crystals of the rhombic $Zn(OH)_2$ described by Fricke and Ahrends [15], who observed this phenomenon when they diluted a concentrated solution of the zincate considerably. As we know, it is easy to obtain a solution that is close, say, to the point 42 (approaching 10% Na_2O; Figure 2), by dissolving amorphous zinc hydroxide in a concentrated alkali. As we dilute this solution with water we successively traverse a series of points lying along the beam: point 42 to the point of 100% H_2O (in Figure 2 the beam from the point 42 to the point for 100% H_2O practically coincides with the dot-dash line from 100% H_2O to $\frac{Na_2O}{ZnO} = \frac{2}{1}$. When dilution is so high that the beam intersects the isotherm EG at a point close to 4% Na_2O, it enters the region of supersaturated solutions where the crystallization of $Zn(OH)_2$ ought to set in. This property of the solutions has been utilized by Fricke and Ahrends [15] as the foundation for their method of securing crystals of $Zn(OH)_2$.

In passing, the formation of crystals of $Zn(OH)_2$ is proof that the position of the point E in the diagram of Figure 2 is correct. The point E, and with it the isotherms EF and EG, are shifted from the 100% H_2O $\frac{Na_2O}{ZnO} = \frac{2}{1}$ beam toward a higher percentage of alkali in the solution. If there were no such shift, it would be impossible to enter the region of solutions supersaturated with respect to crystalline $Zn(OH)_2$, no matter how much any zincate solution were diluted with water.

In an endeavor to obtain solutions richer in zinc, Müller resorted to saturating an alkali by heating it with zinc oxide. These solutions are highly unstable, beginning to throw down crystalline precipitates within a short time. In a series of tests the author prepared several concentrated solutions and seeded them with the crystals obtained in the previous tests. This greatly diminished the percentage of zinc in the solutions, though their alkalinity remained practically unchanged. Thus there is still another isotherm HC in the region of high ZnO concentrations. Müller was unable to determine the composition of the equilibrium bottom phase. According to Scholder [7], however, the isotherm HC represents the trihydrate $[Zn(OH)_3]Na \cdot 3H_2O$.

As Figure 2 indicates, the isotherm HC, plotted from Müller's data (circles with crosses) agrees satisfactorily with Scholder's findings (half-filled circles).

Taking the three components of the system: Na_2O—ZnO—H_2O and allowing for the researches of Müller, Scholder, Fricke, Goudriaan, and others, we have plotted the equilibrium diagram reproduced in Figure 3 and have compiled Table 1, which characterizes this system quantitatively. The diagram mentioned illustrated the equilibrium that exists in the system at 30° between the zincate solution and the bottom phases, whose composition is given by Scholder as follows:

Isotherm	A—A	represents	$NaOH \cdot H_2O$,
"	A—B	"	$[Zn(OH)_4]Na_2$,
"	B—D	"	$[Zn(OH)_4]Na$,
"	H—C	"	$[Zn(OH)_3]Na \cdot 2H_2O$,
"	E—F	"	ZnO and its amorphous hydrate
"	E—G	"	crystalline $Zn(OH)_2$.

The published researches of Fricke [15] and Müller [6] contain some data on the solubility of zinc oxide in potassium hydroxide, but they are too sparse and, what is more, contradictory to serve as a basis for any conclusions whatever.

The sparseness of these findings led us to undertake a more complete experimental determination of the region in which stable solutions of potassium zincate that did not age existed. To secure a clear idea of the behavior of potassium zincate solutions possessing different values of the $\frac{K_2O}{ZnO}$ factor with time, we prepared 150 samples with known integral compositions. The composition of the individual samples was chosen so as to cover evenly the zinc solution region in the K_2O—ZnO—H_2O triangular diagram. This was most conveniently done by the method of cross-sections along the alkali solution (of given concentration)—ZnO beams, as indicated in Figure 4. In this figure there is a separate series of samples for each concentration of the alkali solution.

TABLE 1

Composition of Equilibrium Solutions of Sodium Zincate at 30°

Molar %			ZnO for the isotherm			HC
Na_2O	AA'	A'B	BD	EF	EG	
1	–	–	–	0.08	0.10	–
2	–	–	–	0.20	0.28	–
3	–	–	–	0.52	0.84	–
4	–	–	–	1.00	1.88	–
5	–	–	–	1.52	2.84	–
6	–	–	–	2.08	3.92	–
7	–	–	–	2.56	4.84	4.28
8	–	–	–	3.12	5.92	4.32
9	–	–	6.92	3.64	6.92	4.52
10	–	–	5.76	4.16	8.00	4.88
11	–	–	4.68	4.68	–	–
12	–	–	3.84	5.24	–	–
13	–	–	3.28	–	–	–
14	–	–	3.00	–	–	–
15	–	3.16	2.92	–	–	–
16	–	2.32	–	–	–	–
17	1.76	1.80	–	–	–	–
17.25	0.00	–	–	–	–	–

Previously calculated quantities of the tested zinc oxide or zinc hydroxide were placed in 10-20 test tubes with tapering necks, after which the test tubes were filled with the given quantity of KOH solution and sealed. The samples were kept at 18-24° for more than 60 days, being agitated at periodic intervals. The test tubes that displayed precipitates were opened, and their liquid phases analyzed. Solutions of potassium hydroxide, electrolytic zinc oxide, and crystalline zinc hydroxide $Zn(OH)_2$ were our initial materials.

The alkali solutions were prepared by the Fricke and Jucatis method [16] from fused potassium hydroxide reagent (All-Union Standard, People's Commissariat of Heavy Industry 17374-40).

The pieces of KOH were rinsed in distilled water, and then dissolved in boiled distilled water until saturation was reached. The alkali solutions of the desired concentrations were prepared by diluting the saturated KOH solution, which had been clarified for 10-15 days, with water freed of CO_2. The alkali solutions were kept in glass containers coated on the inside with paraffin; they were decanted by means of siphons that were protected against any access of CO_2. The electrolytic zinc oxide, 00 brand, was prepared by the Mendeleev factory in Leningrad. The outwardly pure white powder of zinc oxide exhibited a loss of 0.047% when calcined at 600°, which was evidence of its nearly complete freedom from CO_2 and H_2O.

The crystalline zinc hydroxide was prepared along the lines of the Fricke and Ahrends method [15]. A solution of KOH (sp.gr. 1.5) was placed in a porcelain beaker and saturated with the initial zinc oxide as it was heated to 130-135°. The remaining solution was decanted and diluted with 15-20 times its volume of water. Ten to fifteen days later the deposited crystalline precipitate was filtered out, washed a few times with cold water and then with hot water, and dried above sulfuric acid. The percentage of water in the resultant preparation ranged from 18.32% to 18.18%, which is close enough to the 18.13% of water in the stoichiometric hydroxide $Zn(OH)_2$.

The zinc in individual check samples was determined electrolytically as described by Reissaus [7]. Verifying tests indicated that, notwithstanding Kolthoff's criticism of the ferrocyanide method [18], this method yields accurate, readily reproducible results if the titration conditions are kept constant. This method is unsuited for mass determinations, however, because of the comparatively bulky apparatus required, not to mention the length of time involved in each determination (at least 1 hour).

We chose the volumetric acidometric method of determining zinc, proposed by Hahn and Hertleb [19], as a more rapid method. This method is based upon the substitution reaction between zinc ions and o-hydroxyquinoline (oxine), in which an equivalent quantity of free acid is produced which is then back-titrated against the alkali. This method proved to be particularly convenient, since it enabled us to determine the percentage of alkali K_2O and of zinc ZnO in the same zincate sample.

The analytical procedure, modified somewhat by us, consisted of the following. A sample of approximately 1 g of the zincate was converted into the sulfate by weighing approximately 10 ml of 1.0 N H_2SO_4 into the same container; then the acid solution was transferred to a 750-ml Erlenmeyer flask. The excess acid was back-titrated in the cold with 0.1 N KOH, methyl red being employed as an indicator. The resultant neutral solution was heated to boiling and a 5% alcoholic solution of oxine was added, using 7 ml of solution per mole of zinc [20]. Boiling lasted 5-10 minutes. The hot solution was poured into a Schott funnel, using no suction; the precipitate was washed with hot water, and the filtrate was titrated with the same KOH solution, with phenol red as an indicator, until a perceptible red color made its appearance. Knowing the total acid present, we can easily calculate the composition of the zincate from the double titration findings; the percentage of water was determined from the difference.

TABLE 2

Solubility of Zinc Oxide in KOH Solutions at 18-22°

Cross-Section No.	Initial KOH solution		Equilibrium zincate solution, molar %			
	Normality	Molar % K_2O	Point Nos.	K_2O	ZnO	Sp. Gr.
V	2.32	2.07	42	2.05	0.182	1.120
			45	2.05	0.182	1.119
IV	4.49	4.00	37	3.97	0.59	1.223
			39	3.98	0.59	1.224
III	5.95	5.30	30	5.15	1.00	1.290
			32	5.15	1.01	1.292
II	9.92	8.86	19	8.73	2.09	1.472
					2.62	1.542
VIII	11.40	10.16	64	9.92		
			67	9.97	2.60	—
I	13.05	11.62	92	11.72	3.37	1.590
			93	11.43	3.20	1.589
VI	14.20	12.62	75	12.13	3.78	1.653
			79	12.11	3.79	1.653

TABLE 3

Solubility of Crystalline Zinc Hydroxide in KOH Solutions at 18-22°

Cross-Section No.	Initial KOH solution		Equilibrium zincate solution, molar %			
	Normality	Molar % K_2O	Point Nos.	K_2O	ZnO	Sp. gr.
IX	2.45	2.18	108	2.14	0.37	1.132
			110	2.13	0.37	—
XII	4.92	4.37	117	4.25	1.52	1.279
			119	4.28	1.53	1.276
XIII	6.23	5.54	126	5.27	2.35	1.352
			130	5.27	2.36	1.351
XIV	7.62	6.77	—	Crystalline precipitate converted into an amorphous one		—
X	9.11	8.10	98	7.44	3.79	1.490
XV	9.58	8.53	—	Crystalline precipitate converted into an amorphous one.		—

We determined solubility in two series of cross sections. In the first series electrolytic zinc oxide served as the initial substance, with crystalline zinc hydroxide $Zn(OH)_2$ used in the second series. The characteristics of the initial and equilibrium solutions of KOH and the zincate are given in Tables 2 and 3 for each cross section.

Part of the $K_2O-ZnO-H_2O$ diagram is shown in Figure 4, the explored cross sections being shown by rays: a KOH—ZnO solution or a KOH—$Zn(OH)_2$ solution. The compositions of the initial mixtures are indicated by circles with the test number alongside them. For the sake of clearness the samples in which not all the sample dissolved or a precipitate had settled out by the time of analysis are denoted by solidly filled-in circles, while the compositions of equilibrium solutions are indicated by circles with crosses drawn inside them.

The ZnO solubility in the sections I-VIII and the $Zn(OH)_2$ solubility in the sections IX-XV, determined by analyzing the liquid phases, enabled us to plot the solubility isotherms of ZnO and $Zn(OH)_2$ in KOH at 18-22°. The shape of these isotherms (Figure 4) is quite similar to that of the isotherms for the solubility of ZnO and $Zn(OH)_2$ in NaOH (Figure 2), and they similarly enable us to delimit a region of stable solutions of potassium zincate from the region of unstable, aging solutions, which throw down secondary precipitates with time, thus being transformed into stable solutions.

The isotherms plotted on a large-scale diagram have been used in compiling Table 4, which gives the molar % of ZnO and K_2O in solutions of potassium zincate that are saturated with respect to ZnO and $Zn(OH)_2$.

The method of individual sealed samples we employed proved to be extremely satisfactory in making approximate determinations of solubility and in observing the dynamics of the establishment of equilibrium within the sample.

The visual characteristic transferred to the diagram in Figure 4 clearly demonstrates that there is no aging of the zincate solutions within the area enclosed by the base of the triangle and the ZnO solubility isotherm, whereas in the region lying above this isotherm the zincate solutions prepared from $Zn(OH)_2$ in the cold or from ZnO by the application of heat are unstable, breaking down to form a liquid phase, whose composition approximates that of the isotherm of stable solutions. This is illustrated, for instance, by the points 140°, 136°, 102°, 147', and 150°, which represent the compositions of the liquid phases of aged solutions, with the same numbers without a prime. The foregoing material on the behavior of sodium and potassium zincate solutions enable us to reach the following practical conclusions.

TABLE 4

Composition of Potassium Zincate Solutions Saturated with ZnO or $Zn(OH)_2$

Molar % K_2O	Molar % ZnO Solubility isotherm		Molar % K_2O	Molar % ZnO Solubility isotherm	
	ZnO	$Zn(OH)_2$		ZnO	$Zn(OH)_2$
1.0	0.0	0.0	8.0	1.84	4.44
2.0	0.20	0.34	9.0	2.22	5.42*
3.0	0.42	0.83	10.0	2.64	6.60*
4.0	0.65	1.44	11.0	3.18	7.80*
5.0	0.90	2.12	12.0	3.72	–
6.0	1.18	2.82	13.0	4.30	–
7.0	1.50	3.56			

*Interpolation

1. Method of Preparing Stable Zincate Solutions

In view of the fact that zincate solutions, no matter how they are prepared, do not throw down precipitates in the region of stable solutions i.e., in the region bounded by the base of the triangle and the ZnO solubility isotherm (Figures 2 and 4), it is most sensible to select a method that makes it possible to prepare zincate solutions most quickly. A method of this sort is the saturation of a concentrated alkali with zinc oxide by heating the latter in it. The composition of the resultant solutions supersaturated with zinc oxide indicates that we have entered the region of unstable solutions located above the ZnO solubility isotherm.

These solutions can be readily stabilized by adding a small quantity of alkali solution (but no water) so as to shift the composition of the resulting mixture into the region of stable solutions.

The control tests we ran to secure strong zincate solutions bore out these conclusions. Thus, 2 solutions of alkali, with 13.5 and 16.5 molar % of K_2O, were saturated with the initial zinc oxide at 130-135°. This yielded 2 zincate solutions, the composition of which were as follows at the instant of their preparation (not shown in Figure 4): Solution 1 - 13.5% K_2O, 5.5% ZnO; Solution 2 - 15.0% K_2O, 6.5% ZnO.

The transparent mother liquors separated from the precipitates soon began to exhibit turbidity, which could be readily eliminated by adding an alkali solution. In the first instance we secured solutions shown in the diagram of Figure 4 by the twin circles and denoted as Nos. 1, 2, and 3. In the second, we secured the solution No. 4. Mixing Solutions Nos. 1 and 4 together yielded Solution No. 5. All five solutions proved to be completely stable, throwing down no precipitate in the course of more than one year. When these solutions were diluted with water, their compositions, changing along the solution – 100% H_2O line, cross the solubility isotherm, enter the metastable region, and throw down amorphous precipitates with time. At even higher dilutions they cross the second isotherm, their composition becoming supersaturated with respect to crystalline $Zn(OH)_2$, with crystals of $Zn(OH)_2$ settling out.

2. Alkaline Method of Leaching Zinc out of Oxide Ores*

We postulate that the properties of the zincate solutions described above do not exclude the possibility of using them in zinc electrometallurgy in which zincate solutions may be produced, as in the processing of oxide zinc ores with alkali solutions followed by their electrolysis or the separation of crystals of zinc hydroxide, similar to the centrifuging process in the production of alumina, followed by regeneration of the alkali solutions.

In conclusion we shall attempt to elucidate the mechanism involved in the aging of zincate solutions, based upon the structure of the zincate molecules in solutions. To do this, let us consider the nature of the ZnO and $Zn(OH)_2$ solubility isotherms in an alkali. As we see in Figure 3, the base of these isotherms on the Na_2O–ZnO side of the triangle is the point corresponding to the factor $\frac{Na_2O}{ZnO} = \frac{2}{1}$, in the first case, and to the factor $\frac{Na_2O}{ZnO} = \frac{1}{1}$ in the second. An explanation for this course of the isotherms is the assumption that zinc oxide or its crystalline hydroxide is converted into the form of two different stoichiometric compounds in solution.

As a matter of fact, let us dissolve ZnO in the alkalies denoted by the letters A, B, and C in the schematic Figure 5. As these solutions are saturated with zinc oxide, the composition of the zincate solutions will shift along the lines A–ZnO, B–ZnO, and C–ZnO. At the instant of saturation of the solution or, as we postulate, at the instant that all the alkali is neutralized by the acid oxide ZnO, aqueous solutions of the stoichiometric zincate $nZnO \cdot mNa_2O \cdot yH_2O$ are formed, represented by the letters a, b, and c, with the constant factor of:

$$\frac{Na_2O}{ZnO} = \frac{m}{n} = \text{const.}$$

It is impossible to saturate these solutions with zinc oxide any further, inasmuch as all the alkali has already been used up in constituting the molecules of the given zincate, the zinc oxide remaining as an unchanged deposit.

* Priority claim No. 373330.

In this instance the ZnO solubility isotherm in an alkali must coincide with the straight line drawn from the 100% H_2O vertex of the triangle to the base with the constant factor of $\frac{Na_2O}{ZnO} = const_1$. A similar position must be occupied by the isotherm for the solubility of the crystalline $Zn(OH)_2$, whose only difference from the former one is the value of the factor $\frac{Na_2O}{ZnO} = const_2$.

Returning now to Figure 3, we find a considerable analogy with the foregoing, the sole difference being that at high dilutions both of the isotherms deviate somewhat from the singular line toward an increase in the percentage of alkali per unit ZnO, which may be readily attributed to hydrolysis of the zincate molecules, producing free alkali and precipitating part of the insoluble "zincic" acid.

As has been stated already, we found that when the isotherm for the solubility of ZnO in NaOH was prolonged until it intersected with the $ZnO-Na_2O$ side of the triangle, the coordinates of the intersection were those of the stoichiometric ratio $\frac{Na_2O}{ZnO} = \frac{2}{1}$ (33.33% ZnO); this made it possible to presuppose that the aqueous solution contains a salt of the tetrasubstituted zincate, the anhydride form of which ought to have the composition of Na_4ZnO_3. The region in which this zincate exists in the solution ranges from the point E to somewhat above the point F', i.e., to a point lying in the supersaturated region. These solutions have a Na_2O content that ranges from 3-11 molar %, the corresponding alkali concentrations being 2.5 to 10 moles/liter. The deviation of the isotherm at the point E from its theoretical position, i.e., from the singular line, is readily attributable to the appreciable hydrolysis of this salt, since, in conformity with the law of mass action, stable solutions of this salt can exist only when an excess of alkali is present. In the region of high dilutions, say 97% water and above, this salt is apparently hydrolyzed to a considerable extent, and the solubility isotherm bends toward 100% H_2O.

Inasmuch as the solubility of ZnO in H_2O is extremely slight, we may confidently expect stable pseudosolutions of ZnO and its hydrates to appear in this part of the diagram; the existence of these latter in alkaline solutions has been set forth repeatedly: by Hantzsch [10], Chatterji and Dhar [11], Dhar and Sen [21], Feitknecht [22], Mehta and Kabadi [23], and others. It is still difficult to render a conclusive verdict concerning the structure of the tetrasubstituted zincate, though in any event Bredig's classical schema, which assumes that the hydroxide's hydrogen is replaced by a metal, does not apply. Regarding the zincate as a coordination compound, we can give the tetrasubstituted zincate the structure of a hydroxo salt, in conformity with the views of Pfeiffer [24]:

$$[ZnO(OH)_4]\,Na_4 \quad \text{or} \quad [Zn(OH)_6]Na_4.$$

Inspection of the diagram in Figure 3 indicates that the tetrasubstituted salt cannot be isolated in the crystalline state, since as the solution is concentrated (decrease in the percentage of H_2O), the less soluble salts, whose composition is given by Müller [6] as $NaHZnO_2$, by Förster [25] as $NaHZnO_2 \cdot 3H_2O$, by Jordis [26] as $ZnO \cdot Na_2O$, by Rubenbauer [27] as Na_2ZnO_2, by Goudriaan [4] as $Na_2ZnO_2 \cdot 4H_2O$, and by Scholder [7] as one of the following hydroxo compounds:

$$[Zn(OH)_3]Na \cdot 3H_2O \text{ and } [Zn(OH)_4]Na_2,$$

settle out of the solution.

In the light of the viewpoint set forth above, the observations of Scholder and Weber [9], who found that crystalline zincates of Ba and Sr were formed when barium and strontium hydroxides were introduced into concentrated zincate solutions are highly interesting. In several instances these zincates had the composition of tetrasubstituted Ba and Sr hexahydroxo zincates: $[Zn(OH)_6]Ba_2$ and $[Zn(OH)_6]Sr_2$, which agrees with our conclusions. It may be that Scholder's trihydrate $[Zn(OH)_3]Na \cdot 3H_2O$ [7] also has the structure of an acid salt: $[Zn(OH)_6]NaH_2$.

As above, we think we can reach a conclusion concerning the structure of the zincate molecule that is in equilibrium with the crystalline $Zn(OH)_2$. The solubility isotherm for $Zn(OH)_2$ starts at the Na_2O-ZnO side of the triangle at the point where $\frac{Na_2O}{ZnO} = \frac{1}{1}$, or 50% ZnO, and hence we can assume that the solution contains hydrolyzed molecules of a disubstituted zincate. The composition of the anhydride form of this zincate must be: Na_2ZnO_2.

If we assume that the structure involved here is again that of a hydroxo compound, one of the following formulas may be attributed to the molecules of the disubstituted zincate: $[Zn(OH)_4]Na_2$, $[ZnO(OH)_2]Na_2$ or $[Zn_2(OH)_8]Na_4$.

It is as yet difficult to state which of these structures is to be preferred, but in any event we can assert that a zincate of the composition $ZnO \cdot Na_2O \cdot 4H_2O$ or $[Zn(OH)_4]Na_2 \cdot 2H_2O$ was formulated by Goudriaan [4], and the

following hydroxo zincates: $[Zn(OH)_4]Na_2$, $[Zn(OH)_4]Na_2 \cdot 2H_2O$; $[Zn(OH)_4]Ba \cdot H_2O$, and $[Zn(OH)_4]Ba \cdot 5H_2O$, and lastly $[Zn(OH)_4]Sr \cdot H_2O$, were isolated in the crystalline state by Scholder and Weber [9], whereas Brinzinger [28] is led by his comparison of the dialysis "coefficients" [29] to conclude that the potassium zincate molecule must have the structure of $[Zn_2(OH)_8]K_4$ in solution, which fully agrees with our conclusions.

The latter molecule, $[Zn_2(OH)_8]K_4$, is a doubled form of the $[Zn(OH)_4]K_2$ molecule and may be regarded as the addition product of a $Zn(OH)_2$ molecule to a molecule of the stable tetrasubstituted zincate $[Zn(OH)_4]K_2$, like the dichromate molecule, which is considered to be the result of the introduction of a molecule of chromic anhydride into the chromate molecule [30]:

$$Na_2CrO_4 + CrO_3 = \left[O-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{Cr}}-O-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{Cr}}-O \right] Na_2$$

Hence, if we assign the structure of $[Zn(OH)_4]Na_4$ to the molecules of the stable zincate and the structure of $[Zn_2(OH)_8]Na_4$, to the molecules of the metastable zincate, the aging of a zincate may be represented by the following chemical equation:

$$[Zn_2(OH)_8]Na_4 \rightleftarrows [Zn(OH)_4]Na_4 + Zn(OH)_2,$$

whence it follows that during the aging process the molecule of the unstable zincate, $[Zn_2(OH)_8]Na_4$, breaks down into a molecule of the stable zincate $[Zn(OH)_4]Na_4$ and zinc hydroxide, which settles out as a precipitate.

In conclusion, I wish to express my indebtedness to Prof. A. P. Okatov for his assistance in this research.

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THE PREPARATION OF POTASSIUM SILICOMOLYBDATES

E. A. Nikitina

Our joint paper with A.G.Kogan [1] described a method of leaching rubudium and cesium out of Solikamsk carnallites with silicomolybdic acid. The theoretical basis for this research involves a systematic study of the equilibria in systems containing potassium, rubidium, and cesium silicomolybdates. There is no literature at all on this problem; references to potassium silicomolybdate are likewise very rare; the octobasicity of silicomolybdic acid $H_8[Si(Mo_2O_7)_6] \cdot xH_2O$ presupposes the feasibility of securing the corresponding number of potassium salts; but all of our observations of silicomolybdic acid indicate that its anion is not very stable, and in the paper we wrote together with A.S.Kokurina [2] we advanced the hypothesis that it is highly unlikely that all eight of the theoretically possible salts of silicomolybdic acid with strong bases can be prepared; as will be evident later on, our supposition has been borne out.

Asch [3] has described the preparation of potassium silicomolybdates (denoted hereafter by s.m.). The author began by preparing a sodium s.m. by introducing molybdic acid into a solution of sodium silicate $Na_2SiO_3 \cdot 9H_2O$. The saturated solution of molybdic acid was evaporated to small volume at 45°, crystals of the tetrasubstituted sodium s.m. settling out when the syrupy liquid crystallized. Asch secured hexagonal prisms of the tetrasubstituted potassium s.m. $K_4H_4[Si(Mo_2O_7)_6] \cdot xH_2O$ by means of a double decomposition reaction with potassium chloride. Asch found that the action of from 4.6 to 8 moles of hydrochloric acid upon this salt resulted in the partial splitting out of a base, and he isolated little yellow tablets of the trisubstituted salt; he obtained the same trisubstituted potassium s.m. by reacting s.m.acid with the tetrasubstituted salt. When he crystallized s.m. acid with 2 moles of KNO_3, he found that the trisubstituted salt separated out together with a small quantity of free s.m. acid. Kono [4] likewise synthesized tri- and tetrasubstituted potassium s.m.

According to Asch, the action of K_2CO_3 upon the tetrasubstituted potassium salt decomposed the coordination compound, yielding potassium trimolybdate; the author's paper gives no figures in support of this conclusion. The literature also contains a reference [5] to the fact that the decomposition of potassium s.m. yields normal potassium molybdate.

EXPERIMENTAL

(Together with E. V. Mogilchenko)

The initial substance, s.m.acid, was prepared by the method developed earlier [6]. In synthesizing the heteropoly acid we used $Na_2SiO_3 \cdot 9H_2O$ (c.p. for analysis) and crystalline MoO_3, which we prepared by dehydrating and then calcining ammonium paramolybdate.

In our earlier paper with A.G.Kogan we found that the yield of s.m. acid can be raised to 90%, based on the MoO_3 entering into the reaction; this high yield was achieved by agitating sodium s.m. very energetically and for a long time (up to 15-20 minutes) in a separatory funnel with sulfuric acid and ether. In the present research we diminished the quantity of H_2SO_4 (sp.gr. 1.5) used in the extraction of the s.m.acid etherate with that acid. The trace of as much as 0.1% SO_4'' in the resultant s.m. acid etherate was eliminated by adding a saturated solution of barium hydroxide to the aqueous solution of the heteropoly acid. After the precipitated $BaSO_4$ had been filtered out, the solution of the s.m. acid was analyzed to determine its percentage of the active principle. This was done by evaporating a sample of the solution (1-2 ml) to dryness on a water bath and then calcining it to constant weight. We used solutions of the s.m.acid, freed of the trace of SO_4'' and containing a known percentage of the heteropoly anion, in preparing the potassium s.m. We employed a neutralization reaction as the basis of our method for preparing these salts. The monosubstituted potassium s.m. was prepared by neutralizing a solution of s.m.acid with the precisely calculated quantity of potassium hydroxide that had been previously likewise dissolved in water; the resultant solution of monosubstituted potassium s.m. was isothermally evaporated in a desiccator over sulfuric acid at a room temperature of approximately 18°. The disubstituted, trisubstituted, and tetrasubstituted salts were prepared by adding the calculated quantities of potassium hydroxide to solutions of the s.m. acid, the solution volumes of which corresponded to one equivalent of KOH in the solution; the equivalents of potassium hydroxide were added at

intervals of 10-15 minutes, with continuous stirring; the solutions of the s.m. acid and of the KOH were cooled with water during the adding of the third and fourth equivalents of potassium hydroxide. All the prepared potassium s.m. were crystallized under the conditions set forth for the monosubstituted salt. The yields of the salts totaled about 80% of the theoretical values. The analyses of the prepared salts are listed in the table below:

Substance	Found %				Moles of H_2O found in the salt	% calculated for anhydrous salt		
	K_2O	SiO_2	MoO_3	H_2O		K_2O	SiO_2	MoO_3
1. Monosubstituted salt $KH_7[Si(Mo_2O_7)_6] \cdot xH_2O$	1) 2.80	3.00	94.20	40.73	40.00	2.59	3.27	94.14
	2) 2.29	3.39	94.32	12.92	25.85	—	—	—
2. Disubstituted salt $K_2H_6[Si(Mo_2O_7)_6] \cdot xH_2O$	1) 5.23	3.02	91.68	10.11	10.64	5.00	3.12	91.78
	2) 4.89	3.13	91.98	13.23	13.92			
3. Trisubstituted salt $K_3H_5[Si(Mo_2O_7)_6] \cdot xH_2O$	1) 7.40	3.10	89.50	7.29	16.20	7.32	3.11	89.57
	2) 7.28	3.17	89.55	7.83	17.33	—	—	—
4. Tetrasubstituted salt $K_4H_4[Si(Mo_2O_7)_6] \cdot xH_2O$	1) 9.47	3.20	87.33	3.20	6.09	9.51	3.04	87.34
	2) 9.60	3.14	87.26	5.97	7.01	—	—	—

The crystals of the monosubstituted salt settled out of solution as thin golden-yellow lamellae. The disubstituted salt crystallizes as thin lamellae and as prismatic crystals. In the first experiment on the preparation of the salt, the hexagonal prismatic crystals predominated, with the lamellar crystals predominating in the second one. The trisubstituted salt crystallized as thin orthogonal lamellae. The tetrasubstituted salt crystallized as hexagonal prisms. The quantities of s.m. acid used in these tests varied from 10 to 250 g.

We then attempted to secure the pentasubstituted potassium salt. This was done by adding a calculated quantity of potassium hydroxide to a solution of the tetrasubstituted salt, both solutions being chilled; isothermal crystallization yielded a white crystalline substance, the supernatant solution being yellow. The white crystals were filtered out, while the yellow solution was subjected to isothermal crystallization again. After several days of standing in the desiccator a gel of silicic acid, which retained the pale-yellow color typical of the s.m. anion because of the adsorption of a small amount of solution of the s.m. salt, settled out of the solution.

Analysis of the white crystals yielded the following results: H_2O - 24.55%; K_2O - 12.87%; SiO_2 - 1.07%; the anhydrous crystals contained 17.42% K_2O and 81.51% MoO_3.

The analysis of the resultant crystals indicates that the addition of the fifth equivalent of potassium hydroxide causes the heteropoly anion to decompose, yielding potassium trimolybdate with potassium silicate as an impurity; the following are the calculated percentages for anhydrous potassium trimolybdate: 17.87% K_2O; 82.13% MoO3.

This synthesis of potassium s.m. shows that s.m. acid is not very stable, so that only four potassium salts can be prepared, in contrast to the stable silicowolframic acid, for which eight potassium salts are known. When the KOH is added gradually, no salts of unsaturated s.m. acids are formed. The fact that a preparation of s.m. acid of precise composition is described only once in the foreign literature is apparently attributable to some error in analysis—failure to drive off the molybdenum trioxide completely during hydrochlorination. Even a minute quantity of residual MoO_3 greatly affects the magnitude of the $\frac{MoO_3}{SiO_2}$ ratio used to evaluate the composition of the s.m. acid. We may add that aqueous solutions of the potassium s.m. we have prepared exhibit an acid litmus reaction.

Analysis of the potassium s.m. involved determination of water, molybdenum trioxide, silicon dioxide, and potassium oxide. About 1 g of the salt was dehydrated by the method described by E.A. Nikitina in the analysis of water in free silico-molybdic acid [7]; the dehydrated sample of salt was hydrochlorinated at approximately 400° in a tubular furnace; the hydrochlorination residue was treated with water and filtered, the water dissolving the potassium chloride, while the SiO_2 remains on the filter; the filter was dried and then burned together with the SiO_2 precipitate and calcined to constant weight; the Cl^- in the filtrate was determined either by Mohr titration with 0.05 $AgNO_3$ or gravimetrically as AgCl; and the percentages of K_2O and of water were calculated from the quantity of KCl found.

SUMMARY

1. The mono-, di-, tri-, and tetrasubstituted potassium salts of s.m. acid have been prepared, the mono- and disubstituted salts being prepared for the first time.

2. It has been established that potassium paramolybdate and a trace of K_2SiO_3 are thrown down when the fifth equivalent of potassium hydroxide is added to s.m. acid.

3. The prepared potassium s.m. are acid salts of octobasic s.m. acid.

4. The synthesis of the potassium salts are evidence that only the ultimately saturated s.m. acid exists, no unsaturated acids being secured under these conditions.

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THE FUSIBILITY DIAGRAM OF THE TERNARY SYSTEM POTASSIUM FLUORIDE–POTASSIUM CHLORIDE–POTASSIUM CHROMATE

I.S.Rassonskaya and A.G.Bergman

The results of research on the liquidus of the ternary system sodium fluoride – sodium chloride – sodium chromate, which is part of the quaternary reciprocal system of the fluorides, chlorides, and chromates of sodium and potassium, have been published previously [1]. The investigation of this reciprocal system constitutes a part of the research program of the laboratory of molten salts, carried out in connection with its exploration of multicomponent systems. The polytherm of the ternary system in question is bounded by three binary systems:

I. KH – KCl [2] is a system with a simple eutectic at 55 mol. % K_2Cl_2, fusing at 605°.

II. KCl – K_2CrO_4 has been investigated by S.F.Zhemchuzny [3], whose research was duplicated by the present authors (Table 1). The fusibility diagram given by S.F.Zhemchuzny consists of two branches that meet at the eutectic point, 658° and 52 mol. % K_2Cl_2. Our findings give the same composition for the eutectic, but a melting point of 650°; the crystallization branch for K_2CrO_4 comprises two curves, representing two heteromorphic modifications of potassium chromate, which meet at a point located at 666° and 50 mol. % K_2Cl_2.

III. KF – K_2CrO_4. The fusibility diagram consists of three crystallization branches: for potassium fluoride, potassium chromate, and the compound $KF \cdot K_2CrO_4$ (i.e., $K_2F_2 \cdot 2K_2CrO_4$), whose fusibility curve exhibits a slight maximum at 768°; the eutectic points are located at 732° and 43 mol. % K_2CrO_4 and 764° and 69 mol.% K_2CrO_4.

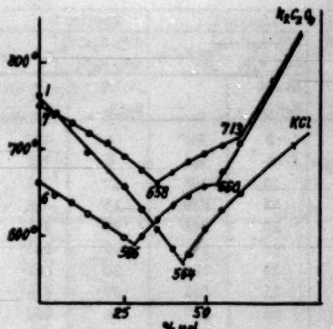

Fig. 1. Internal sections 1, 6, and 7 of the ternary system K‖F, Cl, CrO_4.

The liquidus diagram was plotted by the visual-polythermal method in a platinum crucible. The temperature was measured with a Pt/R – Au/Pd thermocouple. Recrystallized salts were used in this research. The onset of crystallization of the KF and the KCl was spotted very easily by the formation of crystals in the surface of the dark melt; it was harder to fix the onset of crystallization of KF – K_2CrO_4 and K_2CrO_4, since these crystals were formed within the dark molten mass.

The accuracy of the temperature readings at 600° was approximately ± 2°. We plotted the polytherms of five sections running from the KF – K_2CrO_4 side to the KCl vertex, three of which (2, 3, and 4) passed through the compound region, and those of two sections (6 and 7) running from the KF – KCl side to the K_2CrO_4 vertex (Tables 1 and 2, Figures 1 and 2).

Section 4 represents the system $K_2Cl_2 - K_2F_2 \cdot 2K_2CrO_4$, with a eutectic point at 588° and 57 mol.% K_2Cl_2. Small breaks are visible at 612-614° and 654-660° on the branches representing the crystallization of the compound (Sections 2, 3, and 4), which are apparent indications of the presence of some modifications of the compound $KF \cdot K_2CrO_4$.

The regions of crystallization of the components and of the binary compound, characterized by the presence of a rational ridge, are clearly visible in the projection of the crystallization surface of the system KF – KCl – K_2CrO_4 (Figure 3). The data in the literature [4, 5] as well as our own determinations indicate that potassium

TABLE 1

Nos.	Section 1: 35% K_2CrO_4 + 65% K_2F_2 → K_2Cl_2		Section 5: 80% K_2CrO_4 + 20% K_2F_2 → K_2Cl_2		Section 6: 55% K_2F_2 + 45% K_2Cl_2 → K_2CrO_4		Section 7: 75% K_2F_2 + 25% K_2Cl_2 → K_2CrO_4		Binary: $K_2Cl_2 - K_2CrO_4$	
	Mol.% K_2Cl_2	t	Mol.% K_2Cl_2	t	Mol.% K_2CrO_4	t	Mol.% K_2CrO_4	t	Mol.% K_2CrO_4	t
1	0	762°	0	826°	0	661°	0	750°	0	772°
2	5	738	5	798	5	647	5	739	15	742
3	10	718	10	773	10	636	10	730	30	705
4	15	696	15	752	15	624	15	717	45	660
5	20	674	20	724	20	610	20	706	47	650
6	25	655	25	710	25	596	25	690	49	654
7	30	629	30	680	30	596	30	675	51	661
8	35	606	35	664	35	615	35	659	52	664
9	40	582	40	641	40	633	40	672	53	672
10	45	576	45	620	45	643	45	683	55	687
11	50	606	50	650	50	655	50	693	60	718
12	55	627	55	671	55	672	55	702	65	750
13	60	648	—	—	60	704	70	766	70	784

TABLE 2

Nos.	Section 2: 50% K_2CrO_4 + 50% K_2F_2 → K_2Cl_2		Section 3: 60% K_2CrO_4 + 40% K_2F_2 → K_2Cl_2		Section 4: 66.5% K_2CrO_4 + 33.5% K_2F_2 → K_2Cl_2	
	Mol.% K_2Cl_2	t	Mol.% K_2Cl_2	t	Mol.% K_2Cl_2	t
1	0	740°	0	760°	0	767°
2	5	724	5	737	5	742
3	10	708	10	716	10	719
4	15	689	15	692	15	695
5	20	668	20	667	20	676
6	25	647	25	650	25	654
7	30	620	30	627	30	634
8	31	615	32	615	35	620
9	32	607	33	609	36	615
10	33	603	34	607	37	612
11	34	599	35	604	38	610
12	35	594	36	600	39	607
13	37	585	37	591	40	605
14	40	569	39	585	41	602
15	45	585	40	579	42	594
16	50	612	45	597	45	600
17	55	634	55	642	55	650
18	60	654	65	680	70	706

chromate possesses a transition point at 666°. Inasmuch as K_2CrO_4 does not form solid solutions of any perceptible concentrations with either potassium chloride or the compound $KF \cdot K_2CrO_4$ in the case we are dealing with the 666° isotherm of the K_2CrO_4 crystallization region is the boundary between the regions of two modifications of the latter: α = K_2CrO_4 and β = K_2CrO_4.

To check whether various modifications of the compound $KF \cdot K_2CrO_4$ exist, we utilized the heating and cooling curve method, using the N.S.Kurnakov differential-recording pyrometer. Uniformity of heating was achieved by using a potential regulator. The tested composition and the standard (Al_2O_3) were placed in platinum crucibles, and bare Pt—Pt/Rh thermocouples were lowered into the crucibles. Heating curves were plotted both for a 1:1 mixture of unfused KF and K_2CrO_4 and for a 1:1 melt of the two.

The potassium chromate transformation effect appears at 666° on the heating curves for the mixture in the solid state. The heating and cooling curves of the compound $KF \cdot K_2CrO_4$ exhibit only the transformation effect in the solid state at 612° (Figure 4). We also plotted heating and cooling curves for mixtures and melts whose compositions lay in the $KF \cdot K_2CrO_4$ area within the triangle. We found that in addition to the eutectic arrests all the melts exhibited a transformation effect in the solid state at 612°. No effect was observed at 654-660° which apparently indicates there is a homeomorphous transformation at that temperature.[1] Hence, we may conclude from the heating and cooling curves that the $KF \cdot K_2CrO_4$ compound possesses a heteromorphous transformation at 612°. This is reflected in the fusibility diagram of the ternary system (Figure 3). The boundary between the two homeomorphous varieties is shown by the dashed line.

[1] A.G.Bergman is the author of the conclusion regarding homeomorphism.

SUMMARY

A study of the ternary system KF–KCL–K_2CrO_4 by the visual polythermal method and of some areas of the diagram by the method of heating and cooling curves has established that:

1. The surface of the ternary system's liquidus consists of seven crystallization regions: KCl, KF, α-K_2CrO_4, β-K_2CrO_4, α-KF·K_2CrO_4, β-KF·K_2CrO_4 and γ-KF·K_2CrO_4.

2. This system has two eutectic points corresponding to the crystallization of:

a) KCl + KF + γ-KF·K_2CrO_4 – 563° and a composition of 41.5 mol.% K_2Cl_2 + 24 mol.% K_2CrO_4 + 34.5 mol.% K_2F_2;

b) KCl + β-K_2CrO_4 + γ-KF·K_2CrO_4 at 576° and a composition of 42 mol. K_2Cl_2 + 18.5% K_2F_2 + 39.5 mol% K_2CrO_4, and the transition points corresponding to the crystallization of:

c) KF + β-KF·K_2CrO_4 + γ-KF·K_2CrO_4 at 612° and a composition of 26 mol.% K_2Cl_2 + 44 mol.% K_2F_2 + 30 mol.% K_2CrO_4.

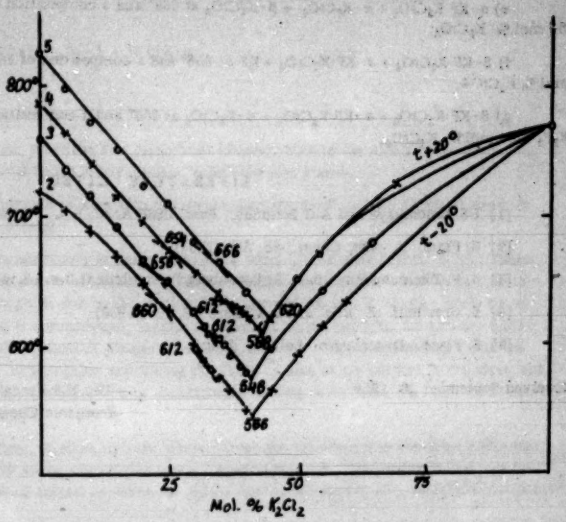

Fig. 2. Internal sections 2, 3, 4 and 5 of the ternary system K‖F, Cl, CrO_4.

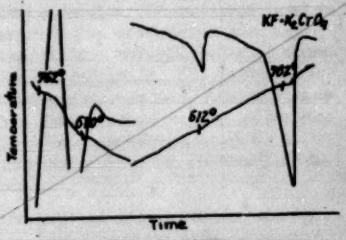

Fig. 4. Differential heating and cooling curves of the compound KF·K_2CrO_4.

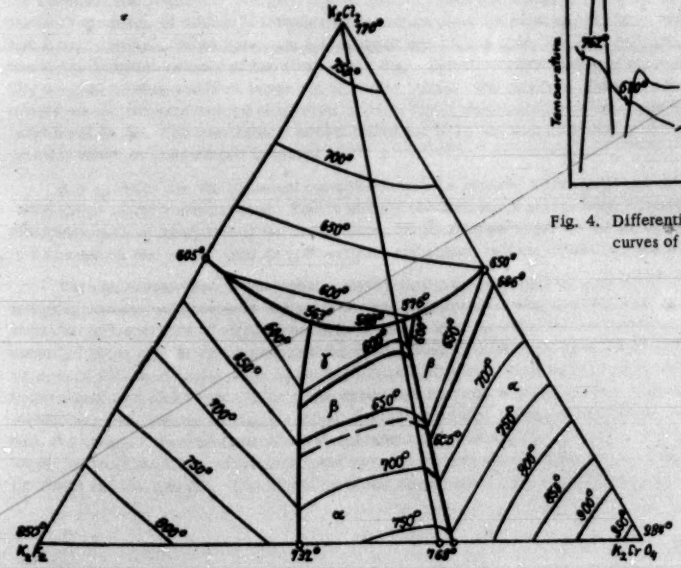

Fig. 3. Polytherm of the ternary system K‖F, Cl, CrO_4.

d) γ-KF·K_2CrO_4 + β-KF·K_2CrO_4 + β-K_2CrO_4 at 612° and a composition of 31 mol.% K_2Cl_2 + 22 mol.% K_2F_2 + 47 mol.% K_2CrO_4;

e) α-KF·K_2CrO_4 + α-K_2CrO_4 + β-K_2CrO_4 at 666° and a composition of 19 mol.% K_2Cl_2 + 25 mol.% K_2F_2 + 56 mol.% K_2CrO_4;

f) β-KF·K_2CrO_4 + α-KF·K_2CrO_4 + KF at 656° and a composition of 16 mol % K_2Cl_2 + 49 mol % K_2F_2 + 35 mol % K_2CrO_4;

g) β-KF·K_2CrO_4 + α-KF·K_2CrO_4 + β-K_2CrO_4 at 656° and a composition of 21 mol.% K_2Cl_2 + 25 mol.% K_2F_2 + 54 mol.% K_2CrO_4.

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THE FORMATION OF DENDRITES IN THE ELECTROLYSIS OF GLASSES

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The formation of dendrites is of great practical and theoretical interest, both in the electrolysis of aqueous and nonaqueous solutions of certain salts and in the electrolysis of solid salts and glasses.

The present paper constitutes an endeavor to ascertain the mechanism involved and the nature of dendrite formation during the electrolysis of solid glasses.

1. The electrolytic nature of the conductivity of glasses was established a long time ago [1, 2, 3]. Those glasses that contain oxides of the alkali elements exhibit the highest conductance. When an electric field is impressed upon a glass, a current passes through it, due to the motion of the ions of the alkali metals. It was shown that when a glass containing sodium oxide is electrolyzed, sodium is deposited at the cathode, its quantity rigidly complying with Faraday's law. Normal electrolysis of glasses is effected, however, only when amalgams of the alkali metals or electrodes made of their molten salts, containing the same cations as are present in the glass, are utilized as electrodes. Under these conditions a glass can be electrolyzed as long as we wish, provided its chemical and physical properties remain unchanged.

When electrodes of platinum, mercury, or other metals, whose oxides are not present in the glass under test, are employed, the current drops off greatly as the electricity passes through the glass. This is due to the fact that the field causes the mobile ions of the alkali metals to leave the region around the anode, thus establishing a poorly conducting layer of glass.

When a metal or a metal amalgam whose oxide is not part of the glass composition is employed as the anode a large percentage of the foreign metal may be introduced into the volume of the glass. This produces a change in the chemical composition of the glass besides causing significant changes in its physical properties. When a substantial percentage of lithium is introduced into sodium glass, for example, the latter turns milky-white and brittle and is easily broken. When potassium is introduced into sodium glass, the glass decrepitates. This phenomenon is due to the different volumes of the alkali metal ions. The alkali meta ls in glass are replaced by silver fairly readily, the glass turning yellow or brown and becoming brittle. The ability of silver to replace the alkali metals when glasses are electrolyzed enabled researchers to make direct measurements of the cation transference number in fused borax [4, 5]. The transference number turned out to be one with an accuracy of 1 to 2%, which indicates the unipolar nature of conductance in glasses.

It is essential that the chemical composition and the physical properties of glasses be conserved during any investigation of their conductance. That is why the conductance of glasses must be measured by the use of active electrodes, such as amalgams of the metals whose oxides are constituents of the glasses tested. We used this method in investigating the conductance of various binary and ternary systems of borax glasses [6].

The electrolysis process proceeded normally during the prolonged electrolysis of all glasses belonging to the foregoing systems, no changes in chemical or physical properties being observed after electrolysis was over. A somewhat different state of affairs was found to prevail when we explored the conductance of borax glasses that contained silver [7]. When we measured the conductance of these latter glasses with electrodes of silver amalgam, we noticed that their conductance was highly unstable after even comparatively brief electrolysis. The electrometer thread fluctuated over a wide range, sometimes moving out of the field of vision entirely. The storage-battery voltage was also unstable during this period, fluctuating wildly. After the test was over, the sample of glass was dark and opaque. Dissemination of metal throughout the volume of the glass is visible with the naked eye. We found that metallic fibers—dendrites—grow from the cathode to the anode during electrolysis, short-circuiting the anode and the cathode. The instability of the electrometer thread and of the battery voltage is due to the

fact that the anode and the cathode are shorted by dendrites, which are then burned out as the result of the passage of a comparatively high electric current through them. Samples of these glasses had so many metallic threads running through them that we were able to pass currents of 0.5 to 0.7 amps through such glass. We also observed dendrites forming when we utilized electrodes made of silver or platinum plates.

The glass sample employed for the test using platinum electrodes exhibited the polarization that is customary for glasses, but after some time had elapsed metallic threads were seen to form within the glass. The thread of the electrometer quivered, and the resistance of the glass was unstable. It should be noted that the strongest and most rapid formation of dendrites occurred in borosilver glasses when they contained more than 40% of silver oxide. When borosilver-alkali glasses were electrolyzed, dendrites began to form when their percentage of silver oxide was lower, which is apparently due to a certain increase in the conductance of these glasses.

We observed an analogous formation of dendrites when we investigated the conductance of glasses that contained monovalent thallium. As the percentage of the metallic oxide in the glass was increased, the passage of the electric current again led to the formation of dendrites. It should be noted that dendrites are produced not only near the electrodes, but also at their periphery. In the latter instance they run mostly in the plane of the glass. The reason for this phenomenon is apparently the nonhomogeneity of the electric field at the edges of the electrodes.

Figure 1 (See plate page 1141) is a microphotograph of a thallium dendrite formed in the plane of the glass. Silver dendrites are of the same shape. The photograph clearly shows that the dendrites' structures differ greatly. In addition to the fine threads, there are areas where a substantial quantity of metal has been deposited. It is characteristic that on the side facing the cathode the base of the dendrite is a thin thread, starting from a point on the surface of the glass. As we travel to the anode, this thread branches out into a widely branched dendrite.

2. The formation of dendrites in glasses containing silver or thallium oxide that we have discovered is typical of salt crystals. Investigations have shown that the electrolysis of solid salts involves an ion transfer that rigidly obeys Faraday's law [1, 4, 8]. It was also noted that in the electrolysis of most salts the metal separating out at the cathode is not deposited uniformly upon the latter, in most instances penetrating into the salt as dendrites, which grow from the cathode to the anode as the current passes. When electrolysis is prolonged, the dendrites grow all the way to the anode, short-circuiting the anode and cathode. At the instance of short circuit a high current passes through the dendrites, burning them out and spraying them throughout the salt. It was noted that the salt was colored brown, red, or blue at these points.

The formation of dendrites during the electrolysis of solid salts constituted one of the most serious obstacles in determining the ion transference numbers in salts, since it is impossible to determine the percentage of the metal in atomized form or in dendrites. It was determined experimentally that dendrites grow extremely slowly during the electrolysis of crystals of silver iodide. This salt was therefore suggested for use as an intermediate salt between the cathode and the salt under test in order to prevent the formation of dendrites in the course of electrolysis [4]. At about the same time S. A. Shchukarev pointed out that silicate cover glasses could be utilized for this purpose [9].

It should be noted at this point that the formation of dendrites likewise interferes with the measurement of the conductance of silver glasses when they contain a high percentage of silver oxide. We used an intermediate sheet of fused borax in measuring conductance in this case to eliminate the formation of dendrites, inserting it between the cathode and the glass sample being tested. No dendrites were formed even when electrolysis was carried out for a long time.

In their study of a sample of rock salt in a constant field, Walther and Inge likewise observed dendrites forming[10]. The authors comment that the growth process of the dendrites can be readily observed in crystals of sodium chloride at temperatures above 350°, it being important to bear in mind that this involves the creation of nonuniformity of the field at the cathode at the start of electrolysis.

A needle, serving as a cathode, was impressed into a rock salt crystal in order to produce such a nonuniformity of the field. When a constant field with a voltage of 8-10 kv was applied, a violet cloud began to appear around the cathode after 10-15 minutes had elapsed, spreading out toward the anode, while reddish sparks were seen inside the crystal. When we examined the crystal after this test, using moderate magnification, thin violet threads were visible, representing the paths along which electrolysis occurred and metallic sodium was deposited. The sodium vaporized as the result of the high current density along this path, yielding a colloidal metal. For the most part these threads were aligned with the edges of the crystal cube. The dendrites within the crystal had the same shape as those we had observed in glasses (Fig. 1).

3. In preparing borax glasses containing silver and thallium oxides our attention was drawn to the fact that these glasses were colored yellow, in contrast to all the other glasses we had handled. The yellow color of silver and thallium glasses grows very much stronger as the percentage of the metal oxide is increased, becoming dark-brown in glasses containing approximately 60% of the oxide.

Glasses that contain silver oxide are coated with an extremely thin film of metallic silver after solidifying and cooling, no matter what their composition. In glasses with a high silver oxide content this film covers the samples with a dense, opaque metallic mirror. As we know, the color of glasses, such as those colored with gold salts, is due to the presence of colloidal particles of gold within the solid glass [11, 12]. The color of the glasses we tested was likewise due to their containing colloidal particles of silver and thallium. With a microscope fitted with a cardioid condenser we succeeded in detecting colloidal particles of metal in the glass. To do this we carefully polished glass samples that contained 70% thallium oxide. The glasses had the shape of thin plates about 1 mm thick. Glycerol was used as the immersion liquid. The microscope field showed the usual picture of colloidal particles, the sole difference being the absence of any Brownian movement. Figure 2 is a microphotograph of colloidal thallium particles observed in the glass plate (see plate page 1141). In the figure we clearly see the particles that lie at the microscope's focus, together with several blurry spots, due to particles above and below the layer in question. As we move the microscope's tube up and down by means of the focusing screw, we can easily see that the colloidal particles are distributed at random throughout the glass.

A much clearer picture is obtained if we use a thin film of glass instead of a plate. Figure 3 is a microphotograph of colloidal silver particles observed in a thin film of borosilver glass.

4. It was stated previously that in preparing glasses containing silver oxide we utilized silver nitrate, which decomposed during the melting of the glass, giving off nitrogen oxides and part of the metallic silver, which settled as drops on the bottom of the crucible. Part of this deposited silver dissolved in the molten glass. When it dissolves, this silver apparently does not yield molecular-disperse solutions in the glass, but dissolves as particles whose dimensions range from amicrons to colloidal particles. We have observed colloidal particles of the metal, both in hard glass and in annealed glass. The minute particles of metal may be aggregated to the dimensions of colloidal particles during the annealing of the glasses, like the particles of gold in the production of ruby glasses.

We found that the solubility of silver rises as the percentage of silver oxide in the glass is increased. The solubility of metallic silver is low in glasses containing up to 30% of silver oxide, and they contain few colloidal particles. This is indicated by the absence of color in these glasses. As the percentage of silver oxide is increased, the color turns from pale-yellow to bright-orange and dark-brown in glasses that contain 60% of silver oxide.

In preparing glasses that contain thallium oxide, we utilized reagents prepared by oxidizing finely pulverized metallic thallium in air at 80-90°. During melting we noticed an increase in the intensity of the glasses' color as the percentage of the metallic oxide was raised. Glasses that contain 60-70% of thallium oxide were identical in appearance, transparent, and dark-brown in color. It may be thought that not all the metal was oxidized during the process of preparing thallium oxide from the metal, but dissolved in the melt during the fusion of the glass, yielding colloidal particles that are responsible for the color of the glasses. To eliminate any introduction of unoxidized thallium into the composition of the glass, we prepared the oxide chemically by reacting a solution of thallium sulfate with barium hydroxide. The precipitated barium sulfate was filtered out, and the solution of thallium hydroxide was evaporated. The deposit of thallium hydroxide was converted into the oxide by heating it in air to 100° in a thermostat. In contrast to the initial glasses, the glasses prepared with this reagent, which contained 60-70% of thallium oxide, were pale-yellow rather than dark-brown, which indicates that in the former case the reagent contained an appreciable percentage of metallic thallium. The pale-yellow color of the glasses prepared from pure thallium oxide is apparently due to the fact that a small portion of the thallium oxide is reduced at high temperature to the metal, which is dissolved in the melt.

If we introduce pieces of metallic thallium into a molten mass of borothallium glass, bubbles of gas appear in the molten mass, which rise to the surface and produce green flashes. After the thallium dissolves in the molten mass, the latter turns dark-brown and much more viscous than before the metal had dissolved in it. When we examine these glasses under a microscope with a cardioid condenser, we see a large number of colloidal particles throughout the glass (Fig. 2).

5. It was pointed out somewhat earlier that we observed no formation of dendrites during electrolysis when we explored the conductance of glasses of widely varying composition. Only in the electrolysis of glasses that contain silver and thallium oxides is the formation of dendrites observed. As has been shown, there are colloidal

particles of silver and thallium throughout these glasses, which are responsible for their color.

It is natural to suppose that the presence of these colloidal metal particles in a solid glass is responsible for the formation of metallic threads and occlusions of dendrites within the glass.

6. Somewhat earlier we pointed out that no dendrites are formed in binary systems of alkali borax glasses no matter how long electrolysis is continued.

We were interested in checking the hypotheses we have just advanced by electrolyzing a borax alkali glass after having dissolved an alkali metal within it. The preparation of such glasses constituted a complicated job. We know that alkali metals react vigorously at high temperatures with boron oxide, displacing the boron, and with silica, displacing the silicon. Moreover, at high temperatures it is extremely hard to introduce an alkali metal into molten glass, as much of it burns up.

The experiments were begun with our preparing a borax sodium glass. This was done by melting borax and electrolyzing it in the molten state, graphite rods being used as electrodes. Electrolysis lasted 15-20 minutes. at a current of some 2 amps.

Some of the metallic sodium deposited at the cathode burned, rising to the surface of the molten mass, though part of it dissolved in the glass. There were minute bubbles throughout all the molten mass. The viscosity of the mass increased substantially, as was the case when silver and thallium were dissolved in glasses that contained oxides of these metals. We endeavored to introduce pieces of metallic sodium into the melt without electrolysis. The resulting picture was the same as when the sodium was introduced by electrolysis.

The melt was kept in the furnace until the glass was formed into sheets, in order to let some of the bubbles escape from the molten mass. Flashes were observed at the surface of the molten mass, due to the burning particles of sodium. Still, the formed and annealed glass contained some bubbles and was pale-yellow in color. The plate of glass was polished and then examined in a microscope equipped with a cardioid condenser. Colloidal particles were visible within the glass, but they were few in number and were hard to observe due to scattering of light by the bubbles left after the molten mass had solidified.

To secure a clearer picture, we prepared thin films of glass, in which the colloidal particles of metal were clearly visible. The overall picture was the same as in the photographs reproduced in Figs. 2 and 3. Our electrolysis of such a hard glass at a temperature of some 300°, using electrodes of sodium amalgam, showed that dendrites grow throughout the glass from the cathode to the anode. The behavior of the electrometer thread and of the battery voltage was the same as that described above. Metallic occlusions were visible within the glass with the naked eye. It should be noted that in this case the growth of dendrites required electrolysis for a much longer time than was needed for the production of silver and thallium dendrites.

Analogous tests were made with borolithium and boropotassium glass. The lithium glass contained 13% of lithium oxide, the potassium glass containing 40% of potassium oxide. The lithium was introduced into the molten glass by electrolysis as well as by adding it as pieces. The potassium was added only by electrolysis. In both instances the molten mass exhibited higher viscosity and a larger number of bubbles.

Dendrites were observed to form during electrolysis of these glasses, as in the case of the sodium glass. The resistance of the glasses and the battery voltage were highly unstable during the process of electrolysis, as was the case in the previous experiments.

A microphotograph of a sodium dendrite is shown in Fig 4 (see plate page 1141). It should be noted that its form differs greatly from that of thallium and silver dendrites. The sodium dendrites are big, dense lamellae. The top of the dendrite, extending toward the anode, is very uneven, consisting of thin, narrow lamellae of true form. The lithium dendrites, photographs of which are shown in Figs. 5 and 6, are of approximately the same shape. These photographs show the appearance of a fracture of a lithium glass sample after electrolysis. The difference between the forms of the dendrites of the alkali metals and those of the silver and thallium dendrites is apparently due to the circumstance that the alkali metals are deposited in the liquid state under the conditions of the experiment (electrolysis of the glass being carried out at approximately 300°), whereas the dendrites of silver and thallium were produced at temperatures below these metals' melting points.

7. We are inclined to attribute the formation of dendrites in the electrolysis of glasses that contain colloidal metal particles within them to the nonuniformity of the glasses' surface in contact with the electrodes, particularly with the cathode. Actually, if there are nonuniformities at the surface of the glass in

Fig. 1.

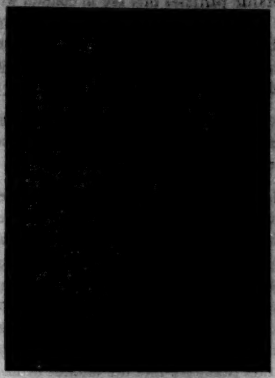

Fig. 2.

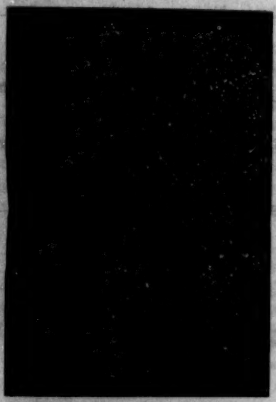

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 6.

the shape of metallic particles that are in contact with the metallic cathode, the current density will rise in the vicinity of these particles. Thus, some of the ions are not directly discharged at the cathode during the process of electrolysis, but rather at these particles within the glass. This results in an increase in the number of particles emerging, leading to a growth of threads within the glass. This increase continues until the metallic thread reaches the anode.

What we have set forth is illustrated by the photographs in Figs. 1, 5, and 6. These photographs clearly show the spot at the surface of the glass in contact with the metallic cathode at which dendrites begin to build up within the glass.

From this point of view we can understand the formation of dendrites during the electrolysis of rock salt in the experiments by Walther and Inge described above. The nonuniformity of the cathode surface, produced artificially by the metallic needle pressed into the salt, results in the formation of dendrites. The formation of dendrites during the electrolysis of salt crystals is usually related to the uneven deposition of metal at the cathode. The unevenness of the crystal surface in contact with the surface of the cathode evidently also is a major factor. There are many fissures and recesses in the surfaces of salt crystals, as was pointed out by Academician A. F. Ioffe long ago. In the course of electrolysis of sheets of salts pressed between the electrodes the metal evolved (sometimes an alkali, liquid metal) fills up the fissures and hollows at the cathode, which then constitute metallic nonuniformities that penetrate into the interior of the salt, like the colloidal particles of metal in the glass discussed by us above. During electrolysis, the metal ions are discharged at these points, the nonuniformity progressing from the surface into the interior of the crystal, producing a dendrite, which reaches the anode as its growth progresses.

In conclusion I wish to express my thanks to Prof. S. I. Sklyarenko for his interest in this research.

SUMMARY

1. It has been shown that the formation of dendrites during the electrolysis of glasses is related to the presence of colloidal metal particles in the glasses.

2. Considerations are set forth concerning the mechanism involved in the formation of dendrites during the electrolysis of solid glasses.

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PHYSICOCHEMICAL INVESTIGATION OF IODINE SOLUTIONS

VIII. THE SYSTEMS: DIIODOTETRAMMINEZINC – IODINE AND DIIODOTETRAMMINECADMIUM – IODINE

Ya. A. Fialkov and F. D. Shevchenko

The study of systems comprising halogens and halides with complex cations is of interest in that it makes it possible to compare the relationships of the halides of simple and complex cations with the halogens and to trace the influence of such factors as a change in the nature and radius of the cation due to the formation of a coordination compound, the nature and number of coordinated groups added to the central atom of the cation, and so forth, upon the formation of the polyhalides and upon their properties.

There are not many references in the literature to this group of problems, the information available being almost exclusively preparative, dealing with the preparation and the description of some of the properties of polyhalides of the foregoing type, such as polyiodides of ammines of various metals (Ni, Co, Cu, Zn, Cd) [1], carbamidates of some trivalent metals [2], and di- and tri-ethylenediamine salts (iodides) of cobalt, nickel, chromium, copper, cadmium, and zinc [3].

As far as physical chemistry is concerned, it is mostly the systems containing ammonium halides or its alkyl (or aryl) substitution derivatives that have been investigated.

In the light of the foregoing considerations we have made an investigation of the $[Ni(NH_3)_6]I_2$ – iodine system [4]; though NiI_2 does not form compounds with iodine in the absence of a solvent (water), thermal analysis indicates that diiodohexammine nickel adds 8 molecules of water, yielding an enneapolyiodide with the composition of $[Ni(NH_3)_6](I_2)_2$. This difference in the ability of nickel iodide and of its hexammine to produce polyiodides must be attributed to an increase in the ionic radius of the cation caused by the change from Ni^{++} to the complex ion $[Ni(NH_3)_6]^{++}$ ion, resulting in an appreciable decrease in the counterpolarization effect upon the polyiodide anion.

Solutions of a polyiodohexamminenickel in molten iodine are good conductors of electricity: the specific conductance rises rapidly with the $[Ni(NH_3)_6]I_2$ concentration, being of the order of 0.1 mho/cm when the concentration of the latter is 3 mol. %. Cryoscopic investigations indicate that the molecules of diiodohexammine nickel and of a polyiodohexamminenickel are associated.

These findings led us to continue with investigations of this sort, using diiodotetramminezinc and diiodotetramminecadmium. In undertaking this research, we had to bear in mind that the halides of ammines of zinc and cadmium are generally less thermally stable compounds than the corresponding ammines of nickel. That was why we could not use diiodohexammine zinc or diiodohexammine cadmium in this research. The dissociation temperature of $[Ni(NH_3)_6]I_2$ at $p = 1$ atm is 235.5°, whereas the corresponding figures for the diiodohexammines of zinc and cadmium are 65° and 107°, respectively, which made it impossible to study their solutions in molten iodine (m.p. 113°). The diiodotetrammines of zinc and cadmium are more stable. Thus, the dissociation temperature of $Zn(NH_3)_4I_2$ is 199° [5].

As was the case with NiI_2, it has not been shown that ZnI_2 and CdI_2 can add iodine by direct interaction between them [1] without the presence of a solvent. The formation of polyiodides of these metals has been observed only in aqueous solutions, though the composition of these coordination compounds is still inadequately known.

The polyiodides of the tetrammines of zinc and cadmium – substances that are apparently more stable than the addition products of iodine to ZnI_2 and CdI_2 – were secured by Ephraim and Mosimann [1] by reacting $ZnSO_4$ or $CdSO_4$ dissolved in aqueous ammonia with an aqueous solution of iodine and potassium iodide. The

[1] Metallic Ni, Z, and Cd do not dissolve in molten iodine [6].

following products were secured: 1) $[Zn(NH_3)_4]I_2 \cdot 2I_2$ – lustrous minute violet-dark-red crystals of lamellar shape; and 2) $[Cd(NH_3)_3H_2O]I_2 \cdot 2I_2$ [1], dark-green (or greenish-black).

EXPERIMENTAL

The iodine was purified as described in previous reports. The specific conductance of molten iodine at 130° was $1.8\text{-}2.0 \cdot 10^{-8}$ mho/cm; m.p. 113.4°.

Diiodotetramminezinc was prepared as follows: a practically saturated aqueous solution of zinc iodide (pure, for analysis) was prepared and then added to an excess of a 20% ammonia solution. The finely crystalline precipitate was recrystallized from the ammonia solution by the use of heat, after which the crystals were filtered out of the mother liquor and washed with alcohol, and then with a mixture of equal volumes of alcohol and ether, and finally dried in a desiccator over solid potassium hydroxide.

Found %: Zn 16.99, 16.84; I 65.35, 65.48; NH_3 17.50, 17.65. $[Zn(NH_3)_4]I_2$.
Calculated %: Zn 16.88; I 65.53; NH_3 17.59.

Diiodotetramminecadmium was prepared by the "dry method": a weighed sample of cadmium iodide (pure, for analysis) was placed in a tube with a bulb at the middle, and gaseous ammonia, which had been dried in towers with potassium hydroxide, was passed through it. The tube was water-cooled externally, as the addition of ammonia to CdI_2 involves the evolution of considerable heat. The mass within the tube increased greatly in volume. Ammonia was passed through the tube until the gain in weight of the tube contents corresponded to the addition of 4 moles of NH_3 to 1 mole of CdI_2. The preparation was obtained as a finely crystalline white powder which smelled faintly of ammonia.

Found %: Cd 25.81, 25.79; I 58.52, 58.57; NH_3 15.35, 15.43. $[Cd(NH_3)_4]I_2$.
Calculated %: Cd 25.88; I 58.44; NH_3 15.68.

The methods of measuring the conductance, the crysocopic determinations, and the like have been described in the preceding report [4].

The $[Zn(NH_3)_4]I_2$ – Iodine System

Thermal analysis. This system could be investigated only up to 27 mol. % (36.3% by weight) of $[Zn(NH_3)_4]I_2$, the solubility limit of the ammine in molten iodine under the given test conditions, by this method. The results of our measurements are given in Table 1 and Fig. 1.

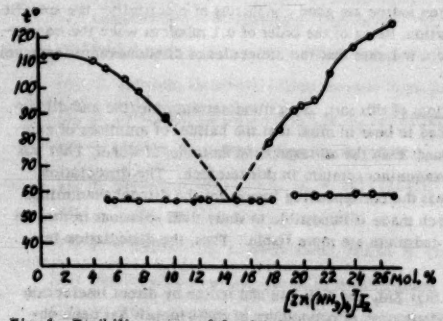

Fig. 1. Fusibility curve of the diiodotetrammine-zinc-iodine system.

We were unable to fix the first arrest points in the concentration range of 10 to 17 mol. % $[Zn(NH_3)_4]I_2$; the eutectic points were well-defined.

Two eutectics, with melting points of 56.0-56.2° and 58.1-58.3°, were found in the $[Zn(NH_3)_4]I_2$–iodine system within the concentration range explored. We see a latent maximum in the fusibility curve at 20-21 mol. % $[Zn(NH_3)_4]I_2$, which is evidence of the formation of a polyiodide with an incongruent melting point having the probable composition of $[Zn(NH_3)_4]I_2 \cdot 4I_2$.

The results of our measurements of conductance are given in Table 2 and Fig. 2.

The $[Zn(NH_3)_4]I_2$–iodine system possesses high conductance, attaining values of the order of magnitude of 0.2 mho/cm when the ammine content exceeded 10 mol. %.

[1] No products any richer in iodine could be obtained, even when a substantial excess of iodine was added.

TABLE 1

THERMAL ANALYSIS OF THE $[Zn(NH_3)_4]I_2$ – IODINE SYSTEM

Molar % of $[Zn(NH_3)_4]I_2$	Arrest points		Molar % of $[Zn(NH_3)_4]I_2$	Arrest points	
	First	Second		First	Second
0.54	111.8°		14.74	–	56.2
1.28	111.2		15.93	–	56.2
3.92	108.8		16.43	–	56.1
5.03	107.1	55.8°	17.66	79.8°	56.0
5.57	106.2	55.9	18.54	83.0	–
6.49	103.4	55.9	19.65	90.8	58.3
7.57	98.7	56.0	20.12	93.1	58.2
9.62	88.3	56.1	20.84	93.9	58.3
10.29	–	56.1	22.00	104.6	58.3
11.36	–	56.1	24.36	115.3	58.1
11.81	–	56.2	25.40	119.8	58.2
12.74	–	56.2	27.20	125.2	58.7

TABLE 2

CONDUCTANCE OF THE $[Zn(NH_3)_4]I_2$ – IODINE SYSTEM

Molar percent of $[Zn(NH_3)_4]I_2$	Specific conductance		Dilution (ml)	Molar conductance at 130°
	130°	140°		
0	$2.07 \cdot 10^{-3}$	$1.96 \cdot 10^{-3}$		
0.31	$1.46 \cdot 10^{-2}$	$1.42 \cdot 10^{-2}$	21168	30.90
0.71	$8.28 \cdot 10^{-2}$	$8.22 \cdot 10^{-2}$	9184	76.04
1.17	$1.51 \cdot 10^{-2}$	–	5603	84.61
2.03	$3.75 \cdot 10^{-2}$	$3.70 \cdot 10^{-2}$	3243	121.6
3.32	$7.66 \cdot 10^{-2}$	$7.68 \cdot 10^{-2}$	2038	156.1
4.67	$1.15 \cdot 10^{-1}$	$1.20 \cdot 10^{-1}$	1481	170.3
7.40	$1.48 \cdot 10^{-1}$	$1.51 \cdot 10^{-1}$	967.5	143.2
10.46	$1.85 \cdot 10^{-1}$	$1.87 \cdot 10^{-1}$	722.5	133.7
12.92	$1.88 \cdot 10^{-1}$	$1.96 \cdot 10^{-1}$	605.5	113.9
15.59	$1.86 \cdot 10^{-1}$	–	520.0	96.72
17.54	$1.87 \cdot 10^{-1}$	$1.91 \cdot 10^{-1}$	472.0	88.24
19.37	$1.87 \cdot 10^{-1}$	–	436.0	81.54

TABLE 3

SPECIFIC GRAVITY OF THE $[Zn(NH_3)_4]I_2$ – IODINE SYSTEM

Molar per cent of $[Zn(NH_3)_4]I_2$	d_4^{120}
0	3.9192
1.91	3.9037
3.57	3.8600
4.82	3.8493
6.50	3.8238
10.56	3.7276
14.89	3.6602

The specific gravities of the solutions of $[Zn(NH_3)_4]I_2$ in molten iodine, which were required for calculating the molar conductance, were determined in a pyknometer with a graduated neck [7]. These measurements are given in Table 3.

The results of our cryoscopic determinations of the molecular weight of diiodotetramminezinc are given in Table 4.

In the $[Zn(NH_3)_4]I_2$ – iodine system the molecular weight of diiodotetramminezinc varies with concentration in the same way as it did in the $[Ni(NH_3)_6]I_2$ – iodine [4] and $(CH_3)_2NI$ – iodine [7] systems: At low concentrations of the ammine in molten iodine, its molecular weight is below the value called for by the formula, though it rises to a value of 438.7 as the $[Zn(NH_3)_4]I_2$ concentration is increased, and then begins to fall again. The reason for this phenomenon will be considered when we discuss our research results.

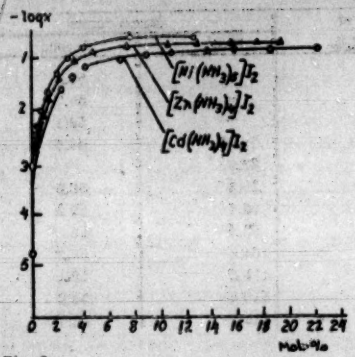

Fig. 2.
Specific conductance of the $[Ni(NH_3)_6]I_2$ – iodine, $[Zn(NH_3)_4]I_2$ – iodine, and $[Cd(NH_3)_4]I_2$ – iodine systems

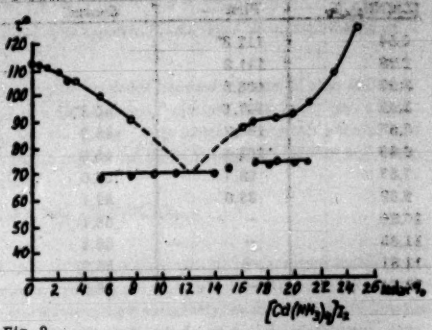

Fig. 3.
Fusibility curve of the diiodotetramminecadmium – iodine system.

TABLE 4

Cryoscopy of the $[Zn(NH_3)_4]I_2$ – iodine System. Mol. Wt. of $[Zn(NH_3)_4]I_2$ = 387.35. Weight of iodine – 34.548 g.

Weight of $[Zn(NH_3)_4]I_2$ sample, g	Molar percent	$\Delta t°$	Molecular weight
0.0507	0.096	0.15	201.0
0.1215	0.23	0.29	245.0
0.1610	0.30	0.34	279.6
0.3464	0.65	0.65	314.7
0.6836	1.28	1.12	359.8
0.8018	1.50	1.26	375.8
1.2706	2.35	1.71	438.7
1.4910	2.75	2.23	394.5
1.8542	3.39	3.51	311.9

The $[Cd(NH_3)_4]I_2$ – Iodine System

See Table 5 and Fig. 3 for the thermal analysis.

The fusibility curve of the $[Cd(NH_3)_4]I_2$ – iodine system, which was explored up to a concentration of 25 mol. % (32.4% by weight), is very similar to the fusability curve of the $[Zn(NH_3)_4]I_2$ – iodine system; here again we find two eutectics with melting points of 70.2-70.4° and 74.1-74.6°, respectively. Unfortunately, the great difficulties we encountered in determining the first arrest points at concentrations that approached the composition of the first eutectic, and the impossibility of fixing them accurately, made it impossible for us to determine the composition of this eutectic. The latent maximum on the fusibility curve of the $[Cd(NH_3)_4]I_2$ – iodine system, which is not very marked, occurs at a concentration of 17-18 mol.% of the ammine. All this leads us to think that in this system (where n may take on several values: 6, 4, etc.) unstable polyiodides $[Cd(NH_3)_4]I_2 \cdot (I_2)_n$ are formed, which are in equilibrium with the products of step-by-step dissociation. The results of our measurements of conductance, specific gravity, and the cryoscopy of the $[Cd(NH_3)_4]I_2$ – iodine system are given in Tables 6, 7, and 8 and Figure 2.

DISCUSSION OF THE RESEARCH RESULTS

Systems that consist of iodine and diiodotetramminezinc or diiodotetramminecadmium have properties that greatly resemble those of the $[Ni(NH_3)_6]I_2$ – iodine system we investigated previously. In all these systems polyiodides are formed that are rich in iodine but are relatively unstable, their stability decreasing from the nickel compounds to those of zinc and cadmium. The formation of an enneapolyiodide has been proved by the presence of a dystectic, though with a slight maximum, on the fusibility curve of the $[Ni(NH_3)_6]I_2$ – iodine system, while the polyiodides of the zinc and cadmium tetrammines are substances with incongruent melting points.

These investigations also proved that the addition of ammonia to zinc and cadmium cations, like its addition to nickel, converts these cations into complex ions and thus sets up the conditions that promote the addition of the iodine molecule to the iodine anions in the outer sphere, for the reasons set forth in the introduction to the present paper.

TABLE 5

Thermal Analysis of the $[Cd(NH_3)_4]I_2$–Iodine System

Molar % of $[Cd(NH_3)_4]I_2$	Arrest points		Molar % of $[Cd(NH_3)_4]I_2$	Arrest points	
	First	Second		First	Second
0.48	111.2°	–	15.23	–	72.4
1.03	110.3	–	16.02	87.8°	–
1.94	108.4	–	16.95	89.3	74.6
2.76	106.9	–	17.91	–	73.9
3.61	105.0	–	18.44	90.6	74.4
5.17	99.7	68.9°	19.71	92.2	74.1
7.83	90.1	70.2	20.92	97.3	74.4
9.47	–	70.2	22.30	101.5	–
10.90	–	70.3	23.12	107.9	–
12.26	–	70.4	24.86	124.6	–
14.10	–	70.3			

TABLE 6

Conductance of the $[Cd(NH_3)_4]I_2$–Iodine System

Molar % of $[Cd(NH_3)_4]I_2$	Specific conductance		Dilution (ml)	Molar conductance at 130°
	130°	140°		
0.19	$3.49 \cdot 10^{-4}$	$3.26 \cdot 10^{-4}$	33836	11.83
0.73	$3.16 \cdot 10^{-3}$	$2.98 \cdot 10^{-3}$	8995	28.42
1.57	$1.36 \cdot 10^{-2}$	$1.32 \cdot 10^{-2}$	4207	57.21
2.44	$2.25 \cdot 10^{-2}$	$2.14 \cdot 10^{-2}$	2740	61.64
3.20	$4.39 \cdot 10^{-2}$	$4.41 \cdot 10^{-2}$	2106	92.47
4.34	$6.21 \cdot 10^{-2}$	$6.36 \cdot 10^{-2}$	1578	98.03
6.94	$9.26 \cdot 10^{-2}$	$9.52 \cdot 10^{-2}$	1022	94.66
9.12	$1.15 \cdot 10^{-1}$	$1.22 \cdot 10^{-1}$	802.2	92.25
11.17	$1.31 \cdot 10^{-1}$	$1.37 \cdot 10^{-1}$	674.5	88.36
13.76	$1.42 \cdot 10^{-1}$	$1.48 \cdot 10^{-1}$	570.3	80.98
15.80	$1.46 \cdot 10^{-1}$	$1.56 \cdot 10^{-1}$	512.3	74.82
18.48	$1.47 \cdot 10^{-1}$	$1.57 \cdot 10^{-1}$	456.8	67.15
22.22	$1.45 \cdot 10^{-1}$	–	402.2	58.31
24.94	$1.46 \cdot 10^{-1}$	$1.55 \cdot 10^{-1}$	373.4	54.51

These systems are likewise very similar as far as their conductance is concerned: the specific conductance of these systems rises rapidly with the ammine concentration attaining values of the order of 0.01 mho/cm even at 1.0–1.5 mol.% while the conductivity is about 0.1 mho/cm at 3.5–8.0 mol.%. As the concentration of the $[Me(NH_3)_n]I_2$ is increased still more, the specific conductance rises much more slowly, becoming constant once it has reached values of 0.15–0.2 mho/cm.

TABLE 7

Specific Gravity of the $[Cd(NH_3)_4]I_2$–Iodine System

Molar % of $[Cd(NH_3)_4]I_2$	d_4^{25}
0	3.9181
2.76	3.8870
5.82	3.8506
11.28	3.7757
15.51	3.7069
25.55	3.5538

In the series of systems containing iodoammines of nickel, zinc, and cadmium, the conductance diminishes from the first of these systems to the last, as shown in Figure 2, where the conductance isotherms of these three systems have been plotted.

It should also be noted that the magnitude of the specific and molar conductances of the systems we have investigated $[Me(NH_3)_n]I_2$–iodine, as well as the shape of their isotherms, closely resemble those of solutions of the iodides of the alkali metals and tetramethylammonium in iodine [8].

This analogy is likewise found in the change of sign and magnitude of the temperature coefficient of conductance with concentration — from a negative value at low concentrations of the iodides to a positive value; the higher the conductance of the system, the lower the concentration at which this change occurs as a rule.

TABLE 8

Cryoscopy of the $[Cd(NH_3)_4]I_2$–Iodine System. Mol. wt. of $[Cd(NH_3)_4]I_2$ = 434.38. Wt. of iodine = 41.372 g.

Weight of $[Cd(NH_3)_4]I_2$ sample, g.	Molar % of $[Cd(NH_3)_4]I_2$	$\Delta t°$	Molecular weight
0.0942	0.13	0.25	190.0
0.2604	0.37	0.53	242.3
0.3975	0.56	0.73	267.1
0.5516	0.77	0.95	286.6
0.8967	1.25	1.33	331.5
1.1832	1.65	1.54	378.0
1.4400	1.99	1.70	416.8
1.6958	2.34	1.84	443.4
1.9803	2.72	1.97	496.2
2.2415	3.07	2.58	428.7
2.6322	3.59	3.64	357.2

A similarly characteristic change in the molecular weight of the iodide (or of the corresponding polyiodide) with concentration is found in all the three $[Me(NH_3)_n]I_2$–iodine systems: the molecular weights calculated from the cryoscopic findings are first lower than the formula values, but rise with concentration to values that exceed those given by the formula, and then begin to drop off.

When we remember the rapid rise in the conductance of these systems even at the low concentrations explored by the cryoscopic method, we must adopt the same conclusion regarding the nature of the electrolytes in these systems that was set forth in our previous paper: the current-conducting particles in solutions of low concentration are the products of the electrolytic dissociation of monomer molecules of the iodides and polyiodides. Then as the system concentration rises, these molecules begin to associate, resulting in an increase in the molecular weight, notwithstanding the large value of conductance (of the order of 0.01 mho/cm).

Subsequently, the increase in the degree of association of the molecules of the polyiodides (and of the iodides) slows down and begins to lag behind the process of electrolytic dissociation, resulting in a renewed drop in the value of the molecular weight.

SUMMARY

1. It has been shown that polyiodides of the composition $[Me(NH_3)_4]I_2 \cdot (I_2)_n$ (n = 4 or 6) are formed in the $[Zn(NH_3)_4]I_2$ – iodine and $[Cd(NH_3)_4]I_2$ – iodine systems.

2. The electrolytic properties of these systems are due to the electrolytic dissociation of the monomer and associated molecules of the polyiodides.

3. The great similarity between the properties of the systems investigated here and those of the $[Ni(NH_3)_6]I_2$ – iodine system is shown, as well as with the iodine solutions of iodides of the alkali metals and alkyl substitution derivatives of ammonium.

4. The research results and a comparison of the iodoammines of nickel, zinc, and cadmium with the simple iodides of these same metals as they react with iodine support the initial postulate of this paper regarding the effect of the change of a simple cation into a complex one upon the ability of the iodine ions in the outer sphere to coordinate iodine molecules, producing polyiodides.

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RESEARCH ON THE COLORED COORDINATION COMPOUNDS OF VANADIUM AND HYDROGEN PEROXIDE

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In our preceding report [1] on the coordination compounds of titanium and hydrogen peroxide we discussed the basic problems involved in determining the composition and properties of coordination compounds containing hydrogen peroxide. The present report sets forth the results of a study of the coordination compounds of vanadium and hydrogen peroxide. The principal objective of our research was a determination of the composition and stability of the coordination compounds in solution under various conditions. Our attention was chiefly focussed on the coordination compound formed in an acid medium. This compound is more highly colored; one of the colorimetric methods for the determination of vanadium is based upon the formation of this compound.

The Effect of the Hydrogen-Ion Concentration Upon the Optical Density of Solutions of Coordination Compounds of Vanadium and Hydrogen Peroxide

We prepared a series of solutions for these measurements in which the concentrations of vanadium and of hydrogen peroxide were held constant at $8 \cdot 10^{-3}$ moles per liter for each of the components. The hydrogen-ion concentration was varied by adding varying quantities of hydrochloric acid, an acetate-ammonia buffer solution being added for values of pH > 4. The optical density was measured with a FM (Pulfrich type) photometer, using a No. 7 light filter, which has a transmission maximum at 465 mμ. Preliminary tests indicated that it is in that region that vanadium coordination compounds with hydrogen peroxide exhibit the strongest absorption of light. Because of the great difference between the color of the solutions in acid and alkali media, the various samples were measured at several different concentrations and thicknesses of the layer. This was done in order to work, if possible, in some mean range of optical density, thus reducing the measurement errors. The molar extinction coefficient (ε) was calculated from the experimental data for convenience in comparing the results, which are listed in Table 1.

TABLE 1

1	$[H^+]$	11^{-11}	10^{-10}	10^{-9}	10^{-8}	10^{-7}	10^{-6}	10^{-5}	10^{-4}	10^{-3}	10^{-2}	10^{-1}	0.3	0.6	1	3
2	ε_1	38	40	43	43	52	144	162	162	162	212	320	345	351	351	351
3	ε_2	21	21	21	21	21	75	162	162	162	14	0	0	0	0	0
4	$\varepsilon_1 - \varepsilon_2$	17	19	22	22	31	69	0	0	0	188	320	345	351	351	351

Direct measurements of the optical density could not be utilized in evaluating our results, since a solution of ammonium metavanadate likewise changes color with its pH. That is why the optical density of solutions of ammonium metavanadate, containing the same buffer solutions, but without any hydrogen peroxide, was measured in a separate series of tests.

Table 1 gives the data for the tests we ran. Line 1 gives the hydrogen-ion concentration; Line 2 the molar extinction coefficient (ε_1) of a solution containing the metavanadate and hydrogen peroxide; Line 3 the molar extinction coefficient of a solution of the metavanadate; and Line 4 gives the difference between the values of the molar extinction coefficients of the solutions of the hydrogen peroxide coordination compound and of the metavanadate solutions.

The following fundamental conclusions may be deduced from the results cited in Table 1. Vanadium forms a compound with hydrogen peroxide in an alkaline medium. The color of this compound is rather weak, being only twice as strong as that of ammonium metavanadate proper.

In the pH range from 7 to 5 the optical density rises sharply in both series, i.e., with and without hydrogen peroxide present. This change must be ascribed principally to changes in state of the metavanadate itself as the pH changes.

As the acidity continues to rise, the optical density of solutions that contain hydrogen peroxide and ammonium metavanadate rises sharply until it reaches a constant value.

This sequence of changes obviously indicates that at least two different coordination compounds are formed in the $V-H_2O_2$ system (in solution.)

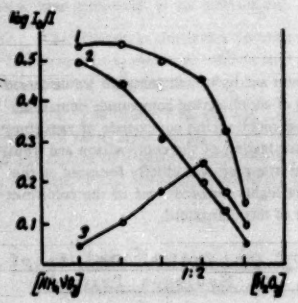
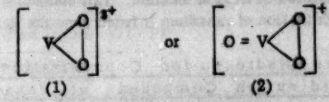


Fig. 1.

The colored compound produced in acid solutions is of the greatest interest for colorimetric determinations. Of all the properties of this compound, what is most striking is its stability in strongly acid solutions. The color is not weakened even in a 6 N acid.

The composition of the colored complex ion of vanadium and hydrogen peroxide formed in an acid medium is usually [2,3] represented by the following formula:



(1) (2)

Thus, it is usually supposed that it is the hydrogen peroxide anion that is the coordinated ion in the colored complex ion. In this case, the color ought to grow fainter as the hydrogen-ion concentration is increased, since the coordinated $O_2^=$ ion must be linked to the hydrogen ions in the molecule of the weak acid H_2O_2.

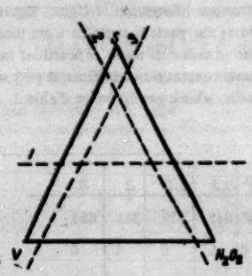


Fig. 2.

The following conclusion must be deduced by analogy with the fuller discussion of this question in connection with the peroxide complex ion of titanium [1].

The fact that the optical density of the solution is not lowered at high $[H^+]$ values may be attributed either to the extremely high stability of a complex ion of Type (1) or Type (2), i.e., its extremely low dissociation constant, or else to the fact that the coordinated group in the complex ion is not the $O_2^=$ ion, but the hydrogen peroxide molecule. In the latter case, i.e., when addition products are formed, the equilibrium should not change as the acidity is raised.

Composition of the Complex Ion Formed In an Alkaline Medium

The intensity of the color of the complex ion formed in an alkaline medium is not very high, whereas the VO_3^- is rather highly colored under these conditions. This circumstance makes it hard to determine the composition of the complex ion. In conformity with the general principle underlying the physicochemical analysis of solutions for determining the composition of a compound, the properties of a series of mixtures must be investigated, consisting of various proportions of equimolar solutions of the reagents.

The optical density of the solutions in one of these series, at pH = 8, is shown by Curve 1 in Figure 1. The ratios of volumes of 0.04 molar solutions of ammonium vanadate and of hydrogen peroxide are plotted along the axis of abscissas. If the reaction components are colorless, with nothing but the reaction product colored, the curve of the optical density of the series of solutions exhibits a maximum at a ratio that corresponds to the composition of the colored compound. The curve does not exhibit a maximum in the given case, however, since one of the components (the metavanadate) is distinctly colored. That is, conclusions concerning the composition of the compound formed must be based solely upon an analysis of the course of the "differences," i.e., the magnitude of the departures from additivity.

Curve 2 in Figure 1 represents the optical density of a series of solutions that contain as much of the metavanadate as the first series, but containing no hydrogen peroxide. The solution of hydrogen peroxide was replaced by a corresponding quantity of water. The difference between the optical density of the solutions of the first series and that of the solutions of the second series is given by Curve 3. Curve 3 displays a maximum at a volumetric ratio of $V:H_2O_2 = 1:2$.

Thus a colored compound is produced in an alkaline medium when 1 gram ion of the metavanadate reacts with 2 moles of hydrogen peroxide. In view of the faintness of the color of this compound it is of no importance for the colorimetric determination of vanadium, so that we made no further investigation of its properties.

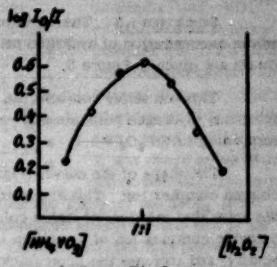


Fig. 3.

Physicochemical Analysis of the Metavanadate–Hydrogen Peroxide System in Acid Solutions

The complex ion of vanadium and hydrogen peroxide produced in an acid medium is highly colored, so that it is of value in the colorimetric determination of vanadium. That is why we have made a fuller study of the composition and properties of this complex ion. The composition of the system may be represented in the form of a ternary diagram (Figure 2), where V denotes the vanadium ion or, generally speaking the ion of pentavalent vanadium in the state in which it exists in strongly acid solutions; H_2O_2 denotes hydrogen peroxide; and S denotes the solvent (a 1 N aqueous solution of hydrochloric acid). The principal types of sections of this system are represented by the lines 1, 2, and 3 in the triangle. Its optical density at 465 mμ was investigated as a property of the system, measurements being made with a photometer.

Section 1. We prepared equimolar solutions ($3 \cdot 10^{-3}$) of the metavanadate and of the hydrogen peroxide. These solutions were mixed together in various proportions so as to keep their aggregate volumes constant. The acidity of all the solutions was identical, being 1 N (in terms of hydrochloric acid).

The results of our measurements of the optical density of this series of solutions are given in Figure 3. Our findings indicate that a peroxide compound of vanadium is formed when 1 gram ion of vanadium reacts with 1 mole of hydrogen peroxide. The shape of the curve is evidence of some dissociation of the colored complex ion.

Section 2. The hydrogen peroxide concentration was varied from $0.6 \cdot 10^{-3}$ up to and including $2 \cdot 10^{-2}$ in a series of solutions whose concentration of the vanadate was kept constant at $2 \cdot 10^{-3}$. The solution acidity was the same in all the tests: 1 N (in terms of hydrochloric acid).

The results of our measurements of optical density are given in Figure 4. The curve exhibits a single bend, at the ratio $V:H_2O_2 = 1:1$.

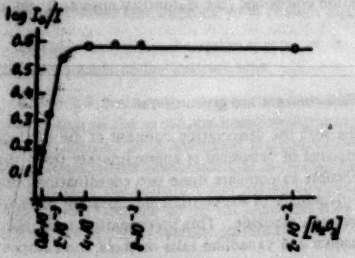


Fig. 4.

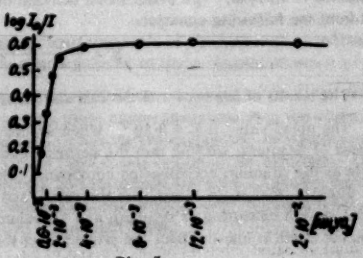


Fig. 5.

The color becomes constant at a certain excess of hydrogen peroxide, undergoing no change as the excess of hydrogen peroxide is increased still further (up to a concentration of $2 \cdot 10^{-2}$ moles of the latter). Thus, there is no reason to suppose that any other coordination compound is produced in the presence of an excess of hydrogen peroxide.

Section 3. The metavanadate concentration was varied from $0.6 \cdot 10^{-4}$ to $2 \cdot 10^{-4}$ in a series of solutions whose concentration of hydrogen peroxide was kept constant at $2 \cdot 10^{-4}$. The results of our optical density measurements are given in Figure 5.

This test series confirms the results secured previously in our investigation of the first and second series of solutions: hydrogen peroxide and vanadium form only a single compound in an acid medium, its composition corresponding to $V:H_2O_2 = 1:1$.

The shape of the curves (Figures 3, 4, and 5) is evidence of a slight, though perceptible dissociation of the colored complex ion. This dissociation is also borne out by a study of the change in color as the solution is diluted. We know that solutions of stable colored complex ions obey Beer's law. Moreover, when we dilute a solution of a peroxide complex ion of vanadium in an acid medium two times, four times, and so forth (without changing their acidity) and increase the layer thickness accordingly two times, four times, and so on, we find that the optical density diminishes. Analogous characteristics of the complex ion of titanium with hydrogen peroxide were discussed at length in the previous paper [1].

When we compare the data on the dissociation of the peroxide coordination compound of vanadium with the data cited above on the stability of the complex ion toward acids, we can reach a conclusion as to the composition of the coordinated group. The colored coordination compound of vanadium and hydrogen peroxide produced in an acid medium is the product of the addition of a hydrogen peroxide molecule $[VO_x(H_2O_2)]^{(z+x)}$. If the colored coordination compound contained a group of type $V<\begin{matrix}O\\O\end{matrix}$, this compound would be unstable in acids (bearing in mind its appreciable dissociation in dilute solutions). Hence, the colored coordination compound of vanadium and hydrogen peroxide that is formed in an acid medium is completely analogous to the corresponding titanium compound as far as its composition and the nature of its bonds are concerned.

A change in the acidity of the solution changes the charge on the ion of vanadium in the solution. In strongly acid solutions, for example, the vanadium moves to the cathode, while in slightly acid solutions it moves to the anode. The presence of hydrogen peroxide has no effect upon the direction in which the vanadium ions move during electrolysis. Moreover, if the coordination sphere contained an $O_2^=$ ion instead of the neutral molecule of hydrogen peroxide, we should expect a change in the charge when the coordination compound was formed. These findings thus corroborate the foregoing conclusion on the composition of the coordination group.

Dissociation Constant of the Colored Coordination Compound of Vanadium (in an Acid Medium)

The dissociation constant of the coordination compound of vanadium with hydrogen peroxide was calculated as described previously for the peroxide compound of titanium [1]. The optical density of a series of solutions containing various concentrations of the metavanadate and hydrogen peroxide was measured. The concentration of the colored coordination compound was determined from a calibration curve plotted from measurements of the optical density of standard solutions that contained an excess of hydrogen peroxide. The concentration of the vanadium not combined into the coordination compound and of the free hydrogen peroxide was calculated from the difference between the initial concentrations of the vanadium ion (or the H_2O_2, respectively) and the concentration of the colored coordination compound. The dissociation constant of the coordination compound (the instability constant) was calculated from the following equation:

$$K = \frac{[VO^{3+}][H_2O_2]}{[(VOH_2O_2)^{3+}]}.$$

The results of our tests and the calculation of the dissociation constant are given in Table 2.

The mean value is $K = 3 \cdot 10^{-5}$. When we compare this value with the dissociation constant of the analogous compound of titanium, we find that the peroxide coordination compound of vanadium is approximately three times as stable as the titanium coordination compound. This makes it possible to compare these two coordination compounds directly, that is, to establish the nature and the order of magnitude of the equilibrium constant experimentally in a system consisting of titanium and vanadium salts and hydrogen peroxide. This investigation is of interest because not much is known about the properties of solutions of titanium and vanadium salts or about the composition

TABLE 2

No.	Concentration, moles/liter		log I_0/I	Concentration, moles/liter			Dissociation constant
	Metavanadate	Hydrogen peroxide	at λ = 465 m	Vanadium peroxide	Uncombined vanadium	Free hydrogen peroxide	
1	$2 \cdot 10^{-4}$	$2 \cdot 10^{-4}$	0.24	$1.4 \cdot 10^{-4}$	$0.6 \cdot 10^{-4}$	$0.6 \cdot 10^{-2}$	$2.2 \cdot 10^{-5}$
2	$2 \cdot 10^{-4}$	$3 \cdot 10^{-4}$	0.26	$1.6 \cdot 10^{-4}$	$0.4 \cdot 10^{-4}$	$1.4 \cdot 10^{-4}$	$3.5 \cdot 10^{-5}$
3	$5 \cdot 10^{-4}$	$5 \cdot 10^{-4}$	0.57	$4.0 \cdot 10^{-4}$	$1.0 \cdot 10^{-4}$	$1.0 \cdot 10^{-4}$	$2.5 \cdot 10^{-5}$
4	$5 \cdot 10^{-4}$	$8 \cdot 10^{-4}$	0.66	$4.5 \cdot 10^{-4}$	$0.4 \cdot 10^{-4}$	$3.4 \cdot 10^{-4}$	$2.4 \cdot 10^{-5}$
5	$8 \cdot 10^{-4}$	$8 \cdot 10^{-4}$	0.90	$6.6 \cdot 10^{-4}$	$1.4 \cdot 10^{-4}$	$1.4 \cdot 10^{-4}$	$2.9 \cdot 10^{-5}$
6	$8 \cdot 10^{-4}$	$10 \cdot 10^{-4}$	0.97	$7.2 \cdot 10^{-4}$	$2.8 \cdot 10^{-4}$	$0.8 \cdot 10^{-4}$	$3.1 \cdot 10^{-5}$

of the respective ions in solution. Vanadium may be present either as a vanadyl cation $-VO^{++}$ or VO_2^{+} – or as a sulfate complex ion in a solution that contains sulfuric acid. Several different forms are likewise possible for titanium. More particularly, it was shown in our previous paper that titanium moves toward the anode when strongly hydrochloric solutions are electrolyzed, i.e., either the $TiCl_5^-$ or the $TiCl_6^=$ ion is formed. Thus, the coordination sphere of peroxide coordination compounds of titantium always contain this or the other ion or group in addition to the hydrogen peroxide molecule. All that our experimental findings prove is that the hydrogen peroxide is added as a H_2O_2 molecule to titanium or vanadium. Neither the charge nor the overall state of the titanium and vanadium ions is affected nor are hydrogen ions displaced from the hydrogen peroxide, i.e., no bonds of the type are produced in a solution in 1M sulfuric acid.

What is most likely is the formation of the complex ions $[TiOH_2O_2]^{3+}$ and $[VOH_2O_2]^{3+}$. More complicated ions may also exist in the solution, however; it may be assumed, more especially, that vanadium polymers are present. In the light of this we were interested in making a direct study of the equilibrium between the two colored coordination compounds.

If we take the above-mentioned simplest forms in which the respective ions can exist in solution, the equilibrium may be represented as follows:

$$TiO^{++} + [VOH_2O_2]^{3+} \rightleftharpoons VO^{3+} + [TiOH_2O_2]^{3+} \qquad (3)$$

$$K_{equib} = \frac{[(TiOH_2O_2)^{3+}][VO^{3+}]}{[TiO^{++}][(VOH_2O_2)^{3+}]}. \qquad (4)$$

The dissociation constants of the respective complex ions are:

$$K_{(TiOH_2O_2)^{3+}} = \frac{[TiO^{3+}][H_2O_2]}{[(TiOH_2O_2)^{3+}]} = 0.9 \cdot 10^{-4}, \qquad (5)$$

$$K_{(VOH_2O_2)^{3+}} = \frac{[VO^{3+}][H_2O_2]}{[(VOH_2O_2)^{3+}]} = 0.3 \cdot 10^{-4}. \qquad (6)$$

Comparing (5) and (6) with (4), we can calculate:

$$K_{equib.} = \frac{[TiOH_2O_2)^{3+}][VO^{3+}][H_2O_2]}{[TiO^{3+}][H_2O_2][(VOH_2O_2)^{3+}]} = \frac{K_{VOH_2O_2}}{K_{TiOH_2O_2}} = \frac{0.3 \cdot 10^{-4}}{0.9 \cdot 10^{-4}} = 0.3.$$

The difference between the absorption spectra of colored peroxide coordination compounds of titanium and vanadium may be conveniently employed for an experimental study of the equilibrium (3). The difference between these absorption spectra is the basis of .. the method described in the literature [4] for determining titanium and vanadium when they are present together.

Figure 6 shows the absorption spectra of the peroxide coordination compounds of titanium and vanadium. An FM photometer of the Pulfrich type, with a set of light filters, was employed in these measurements.

Curve 1 is the absorption spectrum of a solution of the peroxide coordination compound of titanium, while Curve 2 is that of the vanadium coordination compound. We see from these curves that measuring the absorption at 619 mμ enables us to determine the concentration of the vanadium coordination compound, inasmuch as the titanium coordination compound that is present absorbs practically no light in this region of the spectrum. The concentration of the colored coordination compound of titanium may be determined from the difference between the aggregate absorption of the titanium and vanadium coordination compounds with the 466 mμ light filter and the absorption of the vanadium coordination compound with the 619 mμ light filter.

TABLE 3

No.	Concentration in the mixture, moles per liter x 10^{-3}			Log I_0/I at λ = 619 mμ	Equilibrium concentration, moles per liter x 10^{-3}				
	Ammonium metavanadate	Titanium tetrachloride	Hydrogen peroxide		Vanadium peroxide	Titanium peroxide	Uncombined vanadium	Uncombined titanium	Equilibrium K
1	3	3	3	0.35	2	0.7	1	2.3	0.15
2	3	6	3	0.30	1.7	1.0	1.3	5	0.15
3	3	12	3	0.23	1.2	1.5	1.8	10.5	0.20
4	3	18	3	0.19	0.9	1.8	2.1	16.2	0.25
5	5	5	5	0.54	3.5	1	1.5	4	0.12
6	5	10	5	0.44	2.7	1.8	2.3	8.2	0.18
7	5	10	5	0.18	0.8	3.7	4.2	98.0	0.20

It is apparent that both complex ions (the titanium and the vanadium one) will be combined into the colored coordination compound when hydrogen peroxide is present in excess. For that reason, only systems containing an insufficient quantity of hydrogen peroxide and a certain excess of titanium and vanadium are of use in exploring the equilibrium (1).

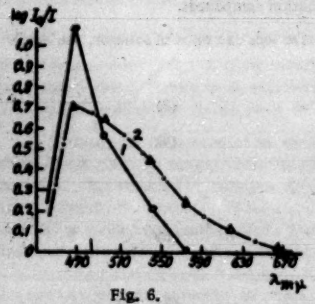


Fig. 6.

The corresponding experimental conditions and the results of our computation of the concentrations of the several components of the equilibrium mixture and of the equilibrium constant are listed in Table 3.

As was pointed out above, the concentrations of the colored coordination compounds were calculated from the optical density measurements. The concentrations of the titanium and vanadium ions that are not combined into a coordination compound were calculated from the difference between the total concentration of titanium tetrachloride (or of the metavandate) and the concentration of the peroxide compound of titanium (or of vanadium).

All measurements were made in solutions containing 1 mole of HCl per liter.

The cited data enable us to take $K_{equiv} = 0.2$ as its mean value.

This value agrees satisfactorily with the value of $K_{equil.} = 0.3$, calculated above from the separate values of the dissociation constants of the coordination compounds.

Thus, our experimental investigation of the equilibrium (3) confirms the values of the dissociation constants we have found. On the other hand, these figures indicate that, despite the comparative complexity of the overall composition of the titanium and vanadium ions in solution, the values of the constants of their peroxide complex ions that we have found may be used to calculate the equilibria in the given system.

SUMMARY

1. Investigation of the optical properties of the solutions by the method of physicochemical analysis has indicated that vanadium forms two colored compounds with hydrogen peroxide. A deeply colored compound is formed in a strongly acid medium ([H^+] from 0.6 to 6N), the composition of which corresponds to a $V:H_2O_2$ ratio of 1:1.

2. In an alkaline medium (pH = 7 and higher) a faintly colored peroxide compound is produced, the composition of which corresponds to a $V:H_2O_2$ ratio of 1:2.

3. Comparison of the perceptible dissociation of the vanadium coordination compound produced in the acid medium with its high resistance to acids indicates that the colored coordination compound of vanadium and hydrogen peroxide formed in an acid medium contains no bonds of the Me type and is the hydrogen peroxide addition product $[VO_x(H_2O_2)]^{(3-2x)}$

4. The dissociation constant has been calculated for the peroxide coordination compound of vanadium formed in a strongly acid medium, $K = 3 \cdot 10^{-8}$.

5. The stability of the peroxide coordination compounds of titanium and vanadium has been compared. The results corroborate the characteristics cited earlier.

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THE PHYSICOCHEMICAL CONSTANTS OF 1,2-CHLOROFLUORETHANE

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The synthesis of 1,2-chlorofluorethane has been described by Razumovsky and Fridenberg [1]. The present research has had as its objective the determination of several physicochemical constants of chlorofluorethane: density, viscosity, surface tension, and vapor pressure at various temperatures. From these findings we have calculated the specific volume, the temperature coefficient of expansion, capillary constant, molecular surface energy, parachor, critical volume, critical temperature, and critical pressure of chlorofluorethane and found that the latter is an unassociated liquid. The atomic volume of fluorine has been computed.

The initial substance was purified by fractional distillation into a column with partial condensation [2]. The column, 90 cm high, was filled with one- and two-turn spirals made of glass thread. A fraction with a boiling point of 51.6-51.9° (735 mm) was collected in the first distillation. In the second distillation, the overwhelming bulk of the substance had a b.p. of 51.8° (732 mm). This fraction was redistilled once more. The resulting preparation was analyzed by the Chablay method [3]. A sealed ampoule containing a weighed quantity of chlorofluorethane was broken inside a test tube containing liquid ammonia. Metallic sodium was added to the solution until it turned blue. The excess sodium was removed, and ammonium nitrate was added in small batches. Then the ammonia was evaporated, care being taken to prevent spattering. The residue was dissolved in water, the chlorine being determined by the Volhard method.

Found %: Cl 23.18, 23.33. C_2H_4FCl. Calculated %: Cl 23.26.

The resultant product was used in our physicochemical measurements. The accuracy of all our measurements was first checked by determining the constants of thoroughly purified benzene; these constants were in agreement with the best figures in the literature, within the limits of possible experimental error.

Density, specific volume, and coefficient of expansion. The density of chlorofluorethane was determined in the 10-30° range in two parallel pyknometers, of 8.5 and 2.0 cc capacity, respectively, with graduations etched on their necks. The precision of thermostat control in this and subsequent measurements was ±0.03°. The precision of the density measurements was approximately 0.05%.

	10°	15°	20°	25°	30°
Density d_4^t	1.192_3	1.184_3	1.176_3	1.168_3	1.160_3
Specific volume v	0.838_9	0.844_9	0.850_7	0.856_8	0.862_1
Coefficient of expansion β	0.00114_9	0.00115_5	0.00117_1	0.00118_7	0.00120_4

$$d_4^t = 1.208_7 - 0.00162t$$

Atomic volume of fluorine. The atomic volume of fluorine may be computed by comparing the molecular volume of chlorofluorethane and dichlorethane at their boiling points and subtracting the difference from the atomic volume of chlorine. The density of chlorofluorethane was obtained by extrapolation from the equation below.

$$V_{C_2H_4FCl} = \frac{98.945}{1.157} = 85.5; \quad V_{C_2H_4FCl}\ \frac{82.46}{1.123} = 73.4;$$

$$\Delta = 85.5 - 73.4 = 12.1$$

Taking the atomic volume of chlorine V_{Cl} as 22.2, we get $V_F = 22.2 - 12.1 = 10.1$ as the atomic volume of fluorine. A result that is close to this value is obtained by comparing the molecular volumes of fluoroform [4] and chloroform: $\Delta = 84.8 - 47.8 = 37.0$; $37.0 : 3 = 12.3$; whence $V_F = 22.2 - 12.3 = 9.9$. Comparing the molecular volumes of dichlorodifluoromethane and tetrafluoromethane [5] yields: $\Delta = 79.5 - 54.3 = 25.2$; $25.2 \div 2 = 12.6$; $22.2 - 12.6 = 9.6$.

When we allow for the atomic volume of carbon $V_C = 14.8$, the molecular volume of tetrafluoromethane [6]

yields: $\Delta = 54.3-14.6 = 39.5$; $39.5:4 = 9.9$. The difference between the molecular volumes of hexafluorethane and tetrafluorethylene [T] yields $\Delta = 85.9-65.8 = 20.1$; $20.1:2 = 10.0$. Thus the calculated values for V_F are: 10.1, 9.9, 9.6, 9.8, 10.0. The mean value of $V_F = 9.9$.

Viscosity. We designed the viscosimeter illustrated in Fig. 1 to measure the viscosity of highly volatile liquids. The viscosity of chlorofluorethane was measured in the temperature range of 15 to 30° and expressed in centipoises. The time required for the water to flow out varied from 74.3 to 103.6 sec, while the corresponding times for chlorofluorethane ranged from 44.7 to 50.0 sec. The viscosity and density of water were taken from the Handbook of Physicochemical Data. The precision of the viscosity determination was 1.0%.

t°	15	16.5	20	25	30
η	0.65_5	0.64_2	0.61_5	0.58_2	0.56_1

Surface tension. The surface tension of chlorofluorethane was measured in the 15-30° range by two methods: the maximum bubble pressure method and the capillary rise method.

We used the layout and apparatus proposed by Rebinder in our determinations by the maximum bubble pressure method. We used thoroughly purified benzene as the liquid to determine the constants of the apparatus. Pressure was measured to within 0.2 mm by a toluene manometer with a mirror scale. The mean of 5-6 measurements was used for each point. The measuring pressure ranged from 70-80 mm. The precision of measurement was approximately ±0.8%. The value of the surface tension of benzene was taken from the Handbook of Physicochemical Data.

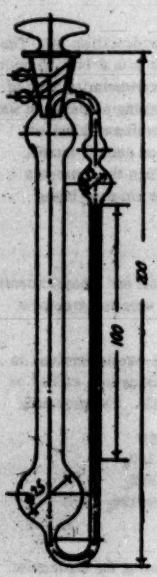

Fig. 1. Viscosimeter.

We ran parallel determinations of the surface tension by the capillary rise method in two carefully calibrated capillaries, with $r_1 = 0.29$ mm and $r_2 = 0.23$ mm. The capillary was placed in a test tube containing chlorofluorethane. The diameter of the test tube was large enough for the meniscus curvature not to affect the accuracy of the measurement of the liquid's rise (h) within the capillary. This rise was measured 3-4 times to ±0.04 mm. The liquid surface was renewed prior to each measurement by forcing the liquid through the capillary, the measurements being repeated within the limits of the stated accuracy. The rise of the liquid was measured as the bottom of the meniscus. This involved the application of a correction. The correction was

$$+\Delta h = \frac{\Delta v}{\pi r^2} = \frac{\pi r^3}{3\pi r^2} = \frac{r}{3}$$

being 0.1 mm (for Capillary No. 1) and 0.08 mm (for Capillary No. 2).

The surface tension was calculated from the formula:

$$\sigma = \frac{hr\,dg}{2},$$

where d is the density of the liquid, g is the acceleration of gravity (980.08 cm/sec²), where r is the radius of the capillary.

The accuracy of measurement was about 0.8 %.

Let us compare the values of surface tension we secured for chlorofluorethane:

	15°	20°	25°	30°
Capillary No. 1	29.34	28.73	27.84	27.14
Capillary No. 2	29.21	28.60	27.94	27.17
Bubble pressure	29.04	28.32	27.63	—
Mean	29.2_3	28.5_5	27.8_8	27.1_5

$$\sigma^t = 31.28-0.138t$$

With these values of σ, we compute the capillary constant a^2 and the molecular energy of chlorofluorethane ϵ where

$$a^2 = \frac{2\sigma}{dg}\ \text{mm}^2; \quad \epsilon = \sigma\left(\frac{M}{d}\right)^{2/3}$$

	15°	20°	25°	30°
a^2	5.03	4.95	4.86	4.78
ϵ	494.2	485.5	474.9	466.1

$$a^2 = 5.31 - 0.018\,t$$

Factor of association. The Eötvös coefficient $k = \frac{\epsilon_1 - \epsilon_2}{t_2 - t_1}$ gives the factor of association of the liquid. It is 2.12 for unassociated liquids. These values of k have been obtained for chlorofluorethane:

$$1.75,\ 2.22,\ 1.78,\ k_{av} = 1.88.$$

Kistyakovsky [8] gives $\frac{Ma^2}{T_b} = 1.16$ for unassociated liquids, where T_b is the boiling point of the liquid (°K) at $p = 760$ mm; a^2 is the capillary constant at that temperature; and M is the molecular weight. The capillary constant of chlorofluorethane, as extrapolated for the boiling point is 4.46. Whence $\frac{82.49 \cdot 4.46}{326} = 1.13$.

It is apparent from the foregoing that chlorofluorethane is an unassociated liquid.

The parachor $[P] = \frac{M\sigma^{1/4}}{d_p - d_v} d_p$ where d_p is the density of the liquid, and d_v is the vapor density taken as 0.0035 (15°) and 0.0033 (30°).

Using the values of σ and d_l for various temperatures, we get: 162.3, 162.5, 162.6, 162.8; mean 162.5.

Calculated from the atomic parachors: 2C = 9.6; 4H = 68.4; Cl = 54.3; F = 26.3.

$$[P]_{C_2H_4FCl} = 158.6.$$

We measured the vapor tension by the static method (cf. Kireev and Popov [9], for example). One feature of our setup is the extremely simple design of the device with a null manometer, which is convenient for use in cases where no especially high accuracy of measurement is required (Fig. 2). The stopcock of the apparatus is lubricated with a grease that is prepared by cautiously heating a mixture of 7 g of glycerol, 5 g of dextrin, and 3.5 g of mannite to the boiling point [10]. The accuracy of reading the manometer did not exceed 0.5 mm. The readings of the manometer were reduced to standard conditions. By way of a check, several points were approached from two sides.

Kireev [11, 12] has proposed an equation that makes it possible to calculate the vapor tension of a substance at other temperatures from measurements of its vapor pressure at two temperatures and from tables of the vapor pressure of hexane. This equation is as follows for chlorofluorethane:

$$\log p = 1.0481 \log P_{hexane} + 0.11914.$$

We cite below the experimental data and the values of the vapor tension P_{calc}, calculated from this equation:

t°	15	20	22	25	30	35	40	45	50	51	52	53	54
P_{mm}	161.0	201.3	218.3	250.1	311.4	383.2	464.4	563.7	682.4	704.3	734.2	770.3	802.8
P_{calc}	162.0	198.8	216.5	250.1	308.0	375.5	464.4	575.4	680.1	701.1	731.0	765.5	800.1

Boiling point. Our measurements of the vapor tension give the boiling point of chlorofluorethane at 760 mm as 52.8 ± 0.1°.

Heat of vaporization. We used three pairs of values of the vapor tension at 40 and 45°, 50 and 45°, and 50 and 52° in calculating the heat of vaporization from the Clausius-Clapeyron equation

$$\lambda = 1.985 \cdot 2.303 \cdot \frac{T_1 \cdot T_2}{T_2 - T_1} \log \frac{P_2}{P_1}$$

We secured the following values for the heat of vaporization of chlorofluorethane: 7.67, 7.77, 7.61, the mean value being 7.68 Cal/mole.

There are numerous semiempirical formulas suggested in the literature relating the heat of vaporization (λ) with the boiling point T_b of unassociated liquids [13].

Comparing the calculated and experimental values of the latent heat of vaporization, Chipman found that the Kistyakovsky equation gave the closest results [14].

Chipman introduced empirical coefficients into this equation for various classes of organic compounds. For halogen derivatives of hydrocarbons: [15]

$$\lambda = 4.578 \cdot 1.030 \log(82.07\,T_b).$$

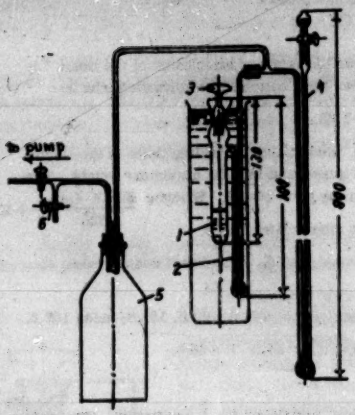

Fig. 2. Apparatus for determining vapor tension (all dimensions in mm).
1 - Test liquid; 2 - theromstated null manometer; 3 - stopcock; 4 - mercury manometer to read the vapor tension; 5 - buffer bottle; 6 - stopcock connecting the apparatus to the atmosphere.

This formula gives $\lambda = 6.80_{Cal}$ [1]

Critical volume. According to Sugden [16], the critical volume is a function of the parachor $v_c = [P]/0.77$. According to Meissner and Redding [17], these two quantities are linked together by the following relationship:

$$v_c = (0.377\,[P] + 11.0)^{1.21}.$$

Taking the values of [P] for chlorofluorethane as 162.5 and 158.6, we obtain 211.0 and 206.0 for v_c from the first formula, the mean being 208.5 cm^3, and 205.9 and 205.4 cm^3 for the second formula, the mean being 205.6 cm^3.

Critical temperature. The Lorentz formula relating the critical temperature T_c to the boiling point T_b gives:

$$T_c = \frac{T_b}{0.64} = \frac{325.9}{0.64} = 509^\circ\,K.$$

The molecular surface energy of a liquid becomes zero at a temperature approximately 6° below the critical temperature. For unassociated liquids:

$$\epsilon = 2.12\,(T_c - 6).$$

The mean value T_c of chlorofluorethane is:

$$T_c = 528.1^\circ K$$

according to this formula.

Meissner and Redding [17] proposed the formula $T_c = T_b + 66 - 11F$, where F is the number of fluorine atoms in a molecule of the compound, for organic compounds that contain halogen atoms. This formula gives $T_c = 514.5^\circ K$. Thus, the T_c of chlorofluorethane probably lies between 510 and 530° K, i.e., 237-257°C.

Critical pressure. Meissner and Redding [17] also suggested a formula linking the critical pressure to the critical temperature and the critical volume:

$$P_c = \frac{20.8\,T_c}{v_c - 8}$$

Whence

$$P_c = 53 \text{ atm.}$$

The authors of the paper assert that the critical values calculated from the suggested formulas correspond to actuality provided the density of the liquid, as determined experimentally, is close to the value calculated from the equation:

$$d = \frac{PM}{K\,82.07\,T},$$

where P is the vapor tension of the liquid; K is a quantity that is a function of the reduced pressure $P_r = P/P_c$ and the reduced temperature $T_r = T/T_c$.

Let us compare $d_{calc.}$ by this formula with $d_{exper.}$:

	15°	20°	25°	30°
d_{calc}	1.17	1.14	1.11	1.13
d_{exper}	1.18	1.17	1.16	1.16

In view of the slight accuracy of the determination of K graphically (from the alignment chart appended to the Meissner and Redding article), the agreement between $d_{calc.}$ and $d_{exper.}$ must be regarded as satisfactory, and the critical values calculated from the formulas the probable ones.

[1] The same paper gives another coefficient, 1.07. With this coefficient $\lambda = 7.07$ Cal.

SUMMARY

Several physicochemical constants of chlorofluorethane have been determined in the 15-30° temperature range: density: $d_4^t = 1.208_7 - 0.00162t$; viscosity: $\eta_{15} = 0.65_5$; $\eta_{20} = 0.61_8$; $\eta_{25} = 0.58_2$; $\eta_{30} = 0.56_1$ centipoise; surface tension: $\sigma^t = 31.28 - 0.138t$ (dynes/cm); factor of association: $\alpha = 1$; parachor: 162.5; vapor tension: $\log p = 1.0481 \log p_{hexane} + 0.11914$; boiling point: 52.8±0.1° (760 mm); heat of vaporization (calculated): 6.8 cal/mole; critical volume (calculated) 209-209 cm^3; critical temperature (calculated) 237-257°; critical pressure (calculated) 53 atm; and atomic volume of fluorine V_F 9.9.

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THE REACTION OF MIXED ORGANOMAGNESIUM COMPOUNDS WITH SALTS OF FLUOSILICIC ACID. III

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During the past few years interest in organosilicon compounds [1] has risen sharply, and they have found important application in practice as the result of the work of Andrianov [2] and Koton [3] for the preparation of valuable materials. We were therefore interested in pursuing our research on the development of a satisfactory method of producing tetrasubstitution derivatives of the monosilanes of the R_4Si type (where R is a hydrocarbon radical). In our researches published previously [4] we described the reaction of sodium fluosilicate with benzylmagnesium chloride, phenylmagnesium bromide, and ethylmagnesium bromide, showing that the yields of the tetrasubstituted monosilanes depends upon the nature of the mixed organomagnesium compound as well as upon the proportions of the reagents. When the reaction is carried out with a large excess of the fluosilicate we found a substantial increase in the yields of tetrabenzylmonosilane, whereas the reaction of a mixed organomagnesium compound with magnesium fluosilicate followed a wholly different course.

These facts served as a basis for a study of the behavior of other fluosilicates with mixed organomagnesium compounds. It was found that potassium fluosilicate differs from the corresponding sodium salt in reacting slowly with benzylmagnesium chloride even at room temperature, giving rise to tetrabenzylmonosilane. The application of heat led to a violent, clearly exothermic reaction, which followed the same course. The yields of the pure tetrasubstituted monosilane were 29-36% of the theoretically possible values (based on the benzyl chloride taken for the reaction), when the substances are used in proportions that nearly satisfy the equation: $4C_6H_5CH_2MgCl + K_2SiF_6 \rightarrow (C_6H_5CH_2)_4Si + 2MgCl_2 + 2MgF_2 + 2KF$.

Barium and calcium fluosilicate did not react with an ether solution of benzylmagnesium chloride at room temperature. Though the application of heat aided the reaction, the yield of tetrabenzylmonosilane still was only 3.9% and 0.77%, respectively.

When heated, potassium fluosilicate reacted with phenylmagnesium bromide, the yield of the organosilicon compound proving to be extremely high – 46.9% of the theoretical. The yield of tetraphenylmonosilane was raised to 25.5% of the theoretical, based upon the organomagnesium compound, by using an excess of sodium fluosilicate.

Thus, potassium fluosilicate must be considered the most suitable salt for synthesizing the tetrasubstituted silanes. When sodium fluosilicate is used, it is advisable to use it in excess.

EXPERIMENTAL

Reaction of potassium fluosilicate with benzylmagnesium chloride. 4.40 grams of potassium fluosilicate, thoroughly pulverized and dried out in a vacuum desiccator over sulfuric acid, was placed in an Erlenmeyer flask with a Grignard reagent prepared from 10.22 g of benzyl chloride, 2.14 g of magnesium and 40 ml of absolute ether. After the ether was driven off, the residue was heated on an oil bath to 160-170° (bath temperature) for 1 hour. Within 3 minutes the temperature within the flask rose precipitately to 196°. The reaction was slowed down by removing the oil bath temporarily. The reaction product was allowed to cool and then treated successively with ether, water, and hydrochloric acid. The ether solution was poured off, and the white precipitate together with the aqueous layer repeatedly extracted with ether (210 ml). The extract was filtered and the ether driven off, followed by the fraction boiling up to 200°, the residue (5.99 g) crystallizing upon cooling. Recrystallization from alcohol and petroleum ether yielded 3.32 g (m.p. 127.5°) of tetrabenzylmonosilane and 0.21 g of dibenzyl (m.p. 52°).

The next experiment was run with the same quantities of reagents, but any rise of temperature inside the flask above 129° was prevented by well-timed cooling. Heating on the oil bath was again continued for 1 hour at a bath temperature of 160-170°. Processing of the reaction products yielded 2.59 g of tetrabenzylmonosilane and 0.19 g of dibenzyl.

The third experiment was run with the same proportions of reagents at room temperature, but without driving off the ether. After 11 days of reaction, the mixture was decomposed with water and hydrochloric acid and extracted with ether, the ether then being driven off and the extract residue being fractionally distilled, first at atmospheric pressure up to 195° and then in vacuo. Finally the residue was recrystallized from alcohol. This yielded 0.23 g of tetrabenzylmonosilane and 0.41 g of crude dibenzyl, plus toluene and a fraction that contained benzaldehyde.

Reaction of potassium fluosilicate with phenylmagnesium bromide. 5.5 g of potassium fluosilicate was added to a Grignard reagent, prepared from 15.7 g of bromobenzene, 2.43 g of magnesium, and 50 ml of absolute ether. After the ether had been driven off, the residue was heated to 147° on an oil bath. A violent reaction set in suddenly, the temperature inside the flask rising to 191° within 5 minutes, notwithstanding the removal of the bath and the application of air cooling. When the temperature within the flask had dropped to 187°, the reaction mixture was heated for 55 minutes on an oil bath (bath temperature 147-175°). During this time the temperature within the flask dropped to 130°. After the reaction product had cooled, it was processed with water, hydrochloric acid, and 20 ml of benzene. Then the benzene layer was poured off, and the residue was extracted repeatedly with benzene (70 ml). The yellowish solid product (7.78 g) left after the benzene had been driven off was washed with hot alcohol and recrystallized from petroleum ether. The melting point (230.5°) and the results of elementary analysis indicated that it was tetraphenylmonosilane, the yield totaling 4.3 g.

Reaction of sodium fluosilicate, taken in excess with phenylmagnesium bromide. 23.5 g of sodium fluosilicate was added to a Grignard reagent prepared from the same quantities of bromobenzene, magnesium, and absolute ether as before. The residue left in the flask after the ether had been driven off was heated for 1 hour, the oil-bath temperature and the temperature within the flask fluctuating within the ranges of 169-175° and 124-129° respectively. The reaction product was treated with 20 ml of benzene, water, and hydrochloric acid. The benzene layer was poured off, and the residue was extracted repeatedly with benzene (100 ml). Recrystallization of the crude product from hot benzene (4.73 g) left after the benzene had been driven off yielded 2 g of pure and 0.34 g of less pure tetraphenylmonosilane, plus 0.13 g of diphenyl (m.p. 70.9°).

Reaction of calcium fluosilicate with benzylmagnesium chloride. An ether solution of benzylmagnesium chloride, prepared from 10.22 g of benzyl chloride, 2.05 g of magnesium, and 50 ml of ether, was distilled on a water bath with 3.64 g of anhydrous calcium fluosilicate. The distillation residue was heated for 1 hour on an oil bath (temperature within the flask: 119-136°). Processing of the reaction product yielded toluene, dibenzyl (0.23 g) and tetrabenzylmonosilane (0.06 g).

Reaction of barium fluosilicate with benzylmagnesium chloride. Two experiments were run: one at room temperature, and the other with heat applied. In the first experiment the ether solution of benzylmagnesium chloride (made from 5.96 g of benzyl chloride, 1.20 g of magnesium, and 29 ml of absolute ether) stood for several days in contact with 3.39 g of barium fluosilicate. Toluene and dibenzyl were found after the products had been processed, no organosilicon compounds being detected.

In the second experiment we used 5.59 g of barium fluosilicate and a Grignard reagent prepared from 10.22 g of benzyl chloride, 2.05 g of magnesium, and 50 ml of ether. After the ether had been driven off, the mixture was heated for 1 hour on an oil bath whose temperature was 160-170°. Processing of the reaction products yielded toluene, dibenzyl (0.34 g), and tetrabenzylmonosilane (0.31 g).

SUMMARY

1. A study has been made of the behavior of potassium, calcium, and barium fluosilicates with benzylmagnesium chloride and of potassium fluosilicate with phenylmagnesium bromide.

2. It has been found that utilizing an excess of Na_2SiF_6 for the production of tetraphenylmonosilane sharply increases the yield (from 5.6% at stoichiometric quantities to 25.5% when the molar ratio of the salt to the phenylmagnesium bromide is 5:4.)

3. Potassium fluosilicate reacts more readily than sodium fluosilicate with benzylmagnesium chloride and phenylmagnesium bromide. The yields of the tetrabenzylsilicon were raised from 20% to 29-36%, while that of tetraphenylmonosilane rose from 5.6% to 46.9% (for stoichiometric proportions of the reagents).

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THE SYNTHESIS AND PROPERTIES OF SOME TRIARYL ALKYL SILANES

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Up to now we know of only a few cyclic C_{16}–C_{22} silanes that are liquids because of the asymmetrical nature of the structure; they are listed in the table below.

No.	Silane	B.p.	Specific gravity
1	$(C_2H_5)_2Si(C_6H_5)_2$ Diethyldiphenylsilane [1]....	305-315°	
2	p-$(C_2H_5C_6H_4\cdot C_6H_5\cdot Si(C_2H_5)_2$ p-Ethylphenyl-diethylsilane [2].....	169-170 at 14 mm	d_4^{15} 0.9830
3	$(C_6H_{11})_2\cdot C_6H_5\cdot SiH$ dicyclohexylphenyl-silane [3].....	340-345	–
4	$(C_6H_{11})_2\cdot C_6H_5\cdot SiC_2H_5$ dicyclohexylphenyl-ethylsilane [3].....	370	–
5	$(C_2H_5)_2C_6H_5\cdot Si\cdot C_6H_4\cdot C_6H_5$ diethylphenyl-xenylsilane [2].....	170 at 14 mm	d_{20}^{20} 0.931
6	α-$C_{10}H_7Si(C_4H_9)_3$ α-naphthyltributylsilane [4]	349-350	d_4^{20} 0.9493
7	α-$C_{10}H_7Si\cdot(C_6H_{11})_3$ α-naphthyltrihexylsilane [4].....	380-384	d_{20}^{20} 0.9936

They are all two or three-ring systems, distinguished by their fairly low viscosity and their specific gravity of less than 1. Continuing the research on the synthesis of silanes containing naphthyl radicals recently published by A.D.Petrov and V.S. Chugunov [4], in the present research we have endeavored to secure four-ring silanes by means of organomagnesium synthesis. Under the conditions described below we succeeded in synthesizing the following: α-naphthyl-di-p-tolylethylsilane and α-naphthyl-di-p-tolyl-n-butylsilane. Both of these substances proved to be highly viscous products (glasses at room temperature), which became mobile at 45-50°, and possessed specific weights in excess of 1. When we tried to synthesize α-naphthyl-di-p-tolyl-tert-amylsilane, we got α-naphthyl-di-p-tolylsilane instead. Taurke [5], Taylor [6], and other researchers secured hydrocarbons of this type by means of the reaction: $HSiCl + 6\,Me + 3RX \rightarrow HSiR_3$, only Cusa and Kipping [3] obtaining phenyldicyclohexylsilane by reacting an excess of cyclohexylmagnesium bromide with phenyltrichlorosilane. They gave

$$C_6H_5(C_6H_{11})_2SiCl + 2C_6H_{11}MgBr \rightarrow$$

$$\rightarrow C_6H_{11}\text{–}C_6H_{11} + MgBrCl + C_6H_5(C_6H_{11})_2SiMgBr \rightarrow C_6H_5(C_6H_{11})_2SiH$$

as the last stage of this reaction, finding that the third cyclohexyl radical cannot enter the silane molecule because of steric hindrances.

In our experiment the reaction was as follows:

$$\alpha\text{-}C_{10}H_7(C_6H_4CH_3)_2SiX + 2BrMg\text{–}\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{\overset{|}{\underset{|}{C}}}}\text{–}CH_2\text{–}CH_3 \rightarrow MgBrX +$$

$$CH_3\text{–}\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{\overset{|}{\underset{|}{C}}}} = CH\text{–}CH_3 + CH_3\text{–}\underset{\displaystyle CH_3}{\overset{\displaystyle H}{\overset{|}{\underset{|}{C}}}}\text{–}CH_2\text{–}CH_3 + \alpha\text{-}C_{10}H_7(C_6H_4CH_3)_2SiMgBr \rightarrow \alpha\text{-}C_{10}H_7(C_6H_4CH_3)_2SiH.$$

It is obvious that it is impossible to introduce two such sterically difficult radicals as α-$C_{10}H_7$ and

$$\text{–}\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{\overset{|}{\underset{|}{C}}}}\text{–}CH_2\text{–}CH_3$$

with the aid of Mg.

EXPERIMENTAL

1. α-Naphthyl-di-p-tolylethylsilane. We used α-naphthyltriethoxysilane, produced by the E.Khotinsky–V. Serezhenkov method [7], as our initial material. The introduction of two tolyl radicals required a considerable excess of p-bromotoluene and Mg, with the reaction carried out in boiling toluene. When the excess of the aryl halide and Mg was diminished to 100%, we got a mixture of α-naphthyl-p-ditolylethoxysilane and α-naphthyl-p-tolyldiethoxysilane under the stated temperature conditions. Substitution of the last ethoxy group was even harder; even when we boiled a sixfold excess of ethyl bromide in isoamyl ether we got nothing but a mixture of α-naphthyl-p-ditolylmonoethoxysilane and the corresponding tetrasubstituted silane. Only a reprocessing of this mixture with a sixfold excess of C_2H_5Br under the same conditions yielded the pure tetrasubstituted silane.

Used: 29 g of naphthyltriethoxysilane, 171 g of p-bromotoluene, 23 g of magnesium, 400 ml of ether, and 200 g of toluene.

α-Naphthyltriethoxysilane was poured into Mg-p-tolyl bromide at room temperature; then the ether was driven off and replaced by toluene, in which the reaction mixture was heated on an oil bath for two hours. The reaction product was decomposed, first with water (using efficient cooling), and then with dilute H_2SO_4, until all the precipitate had dissolved. The toluene was driven off, and the fraction boiling over 242° was distilled in a 2-mm vacuum; Fraction 1, up to 140° – 6 g; Fraction 2, 140-236° – 5 g; Fraction 3, 232-238° – 27 g; and Fraction 4 (residue) – 12 g. Fraction 1 crystallized in part.

Analysis of the crystals with a m.p. of 121°:
0.1322 g subs.: 0.4464 g CO_2; 0.1322 g H_2O. Found %: C 92.09; H 7.81. $C_{14}H_{14}$. Calc.%: C 92.27; H 7.73.

The analysis findings and the melting point indicated that the solid substance was di-p-tolyl.

Fraction 3, the yield of which was 70%, was a thick, not very mobile green liquid; its b.p. was 234-236° at 2 mm after redistillation.

0.1424 g subs.: 0.4282 g CO_2; 0.0912 g H_2O. 0.6100 g subs.: 0.0940 g SiO_2. 0.1250 g subs: 20.7 ml 0.1 N $Na_2S_2O_3$ (by the Kreshkov and Nessonova method [8]). Found %: C 82.03; H 6.86; Si 7.23; OC_2H_5 11.86. $C_{24}H_{24}SiOC_2H_5$. Calculated %: C 81.62; H 6.86; Si 7.34; OC_2H_5 11.78.

Thus, the 234-236° (2 mm) fraction was α-naphthyl-di-p-tolylmonoethoxysilane [α-$C_{10}H_7(CH_3C_6H_4)_2SiOC_2H_5$].

We used: 9.2 g of Mg, 44 g of C_2H_5Br, 25 g of α-naphthyl-di-p-tolylmonoethoxysilane, 150 ml of diethyl ether, and 150 ml of isoamyl ether in the synthesis of α-naphthyl-di-p-tolylethylsilane.

To ethylmagnesium bromide dissolved in ether we added α-naphthyl-di-p-tolylmonoethoxysilane, after which the diethyl ether was replaced by isoamyl ether, and the reaction mixture was heated to the boiling point of the isoamyl ether on an oil bath for 6 hours.

The product was decomposed in the usual manner and the isoamyl ether driven off, leaving 22 g of a fraction with a b.p. of 224-230° at 1.5 mm, which still contained some α-naphthyl-di-p-tolylmonoethoxysilane, to judge by the analysis findings. The fraction was reprocessed with an excess of C_2H_5MgBr (9.2 g of Mg and 44 g of C_2H_5Br) under the conditions set forth above in order to effect complete replacement of the ethoxy group. After decomposition, we secured 17 g of a fraction with a b.p. of 224-226° at 1.5 mm. At room temperature it was a glass, which became mobile at 45-50°.

d_{21}^{21} 1.0798.

0.1328 g subs.: 0.4142 g CO_2; 0.0866 g H_2O. 0.5234 g subs.: 0.0828 g SiO_2. Found %: C 85.05; H 7.20; Si 7.46. $C_{28}H_{26}Si$. Calculated %: C 85.18; H 7.15; Si 7.67.

2. α-Naphthyl-p-ditolyl-n-butylsilane was synthesized under the conditions specified above, the yield totaling 20 g (80% of the theoretical).

B.p. 227-229° at 1.5 mm; d_{23}^{23} 1.0697.
0.1306 g subs.: 0.4066 g CO_2; 0.0870 g H_2O_2. 0.6074 g subs.: 0.0992 g SiO_2. Found %: C 84.95; H 7.45; Si 7.32. $C_{28}H_{32}Si$. Calculated %: C 85.20; H 7.67; Si 7.11.

3. α-Naphthyl-p-ditolylsilane. Initial materials: 17.5 g of Mg, 83 g of tert-amyl chloride, 20 g of α-naphthyl-p-ditolylmonoethoxysilane, 400 ml of diethyl ether, and 150 ml of isoamyl ether. The ethoxy group was replaced at once in this case, no further processing of the reaction product with tert-amylmagnesium chloride being required. The thick liquid with a b.p. of 229-231° at 1.5 mm we secured was more like $C_{34}H_{32}Si$ than $C_{29}H_{28}Si$, to judge by the analysis findings.

0.1350 g subs.: 0.4220 g CO_2; 0.0868 g H_2O. 0.6124 g subs.: 0.1038 g SiO_2. Found %: C 85.20; H 7.21; Si 7.95. $C_{29}H_{28}Si$. Calculated %: C 85.23; H 7.90; Si 6.87. $C_{34}H_{32}Si$. Calculated %: C 85.20; H 6.53; Si 8.27.

The presence of hydrogen instead of a tertiary amyl group in the final product was also proved by treating it with a 20% solution of KOH and acetone (by the Cusa and Kipping method), slow decomposition with the evolution of hydrogen ensuing.

SUMMARY

1. α-Naphthyl-di-p-tolylethylsilane, α-naphthyl-di-p-tolylbutylsilane, α-naphthyl-di-p-tolylmonoethoxysilane, and α-naphthyl-di-p-tolylsilane have been synthesized for the first time.

2. It has been shown that organomagnesium synthesis cannot be employed to introduce two sterically hindered radicals — α-naphthyl and tert-amyl — into a silane molecule.

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MOLECULAR COMPOUNDS OF $ZnCl_2$ WITH ALCOHOLS

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Zinc chloride is widely used as a catalyst in various alkylation reactions. There are many papers [1] on the alkylation of phenols, amines, and aromatic hydrocarbons with alcohols. The mechanism involved in these syntheses has not been investigated systematically up to now, however. Some researchers consider that $ZnCl_2$ acts in these syntheses as a dehydrating agent. Others [3], without any justification, compare its action with that of $AlCl_3$, H_2SO_4, and other acid catalysts.

We believe that the isolation and study of the intermediate products formed during the reaction are of great importance in clearing up the mechanism involved in these syntheses. We therefore undertook an investigation of the reaction of alcohols with $ZnCl_2$ with the objective of ascertaining wherein $ZnCl_2$ differed from or resembled other condensing agents.

In order to learn whether zinc alcoholates could be formed as intermediate products in alkylation with alcohols, we made a study of the reaction of n-butyl and isoamyl alcohols with $ZnCl_2$ under alkylating conditions. A current of anhydrous nitrogen was passed through a mixture of the alcohol and $ZnCl_2$ as it was heated first to 60-80° and then to 170-175°. After the nitrogen had passed through the reaction mass, it was passed through a bottle containing a concentrated solution of $AgNO_3$. No HCl was evolved at all.

Convinced that it was unlikely that zinc alcoholates were produced under these conditions, we then made a study of the products secured when $ZnCl_2$ reacts with alcohols. We investigated the reactions of $ZnCl_2$ with methyl, ethyl, n-propyl, n-butyl, isopropyl, and isoamyl alcohols. We also made a study of similar reactions with ethylene glycol and cyclohexanol. The reactions were carried out at 110-170°. Appropriate processing of the products of the reaction between $ZnCl_2$ and the alcohols yielded coordination compounds, the composition of which was established by analysis. It was found that the alcohols and the $ZnCl_2$ combined in these coordination compounds in equimolar proportions, yielding $ROH \cdot ZnCl_2$. In the case of cyclohexanol we secured a crystalline compound, $(C_6H_{11}O)_2 \cdot ZnCl_2$. The other reaction products were thick, oily liquids with a peculiar odor, which were highly hygroscopic and unstable and possessed strongly acid properties.

Investigation of the pH of aqueous and alcoholic solutions of $ZnCl_2$ indicated that a change in the $ZnCl_2$ concentration greatly affects the pH. For instance, when the $ZnCl_2$ concentration in C_2H_5OH was 0.44 M, the pH was 4.59, while at 4.9 M the pH was 2.06.

According to Meerwein [4], the acidic properties of such compounds are due to the formation of complex acids of the following type:

$$ZnCl_2 + 2H_2O \rightleftharpoons [ZnCl_2 \cdot (OH)_2]H_2 \rightleftharpoons [ZnCl_2(OH)_2]^- + 2H^+$$

Hence, it must be supposed that alcohols also yield similar acids: $[ZnCl_2 \cdot (OR)]H$, $[ZnCl_2 \cdot (OR)_2]H_2$. These coordination compounds are cleaved at certain temperatures, yielding olefins, ethers, aldehydes, hydrogen, water and zinc oxychloride

Then we investigated the catalytic activity of these acidic coordination compounds in alkylation, acylation, and esterification reactions. Condensation of benzoyl chloride with toluene in the presence of $[ZnCl_2 \cdot C_2H_5O]H$, $[ZnCl_2 \cdot (C_6H_{11}O)_2]H_2$, or $[ZnCl_2 \cdot OH]H$ at 40-70° results in the formation of 4-methylbenzophenone (25-35%). These reactions do not take place under these conditions when $ZnCl_2$ is used.

Benzene was alkylated with n-butyl chloride at 80-85° in the presence of $[ZnCl_2 \cdot C_2H_5O]H$, yielding a mixture of butylbenzenes (25%). As we noted earlier [5], alkylation with alkyl chlorides takes place only at much higher temperatures (150-200°) when $ZnCl_2$ is used.

When we alkylated toluene with trimethylethylene in the presence of $[ZnCl_2 \cdot C_2H_5O]H$ we secured a mixture of isomeric amyltoluenes (20%); no reaction took place with $ZnCl_2$.

The reaction of ethyl alcohol with glacial acetic acid in the presence of $[ZnCl_2 \cdot C_2H_5O]H$ or $[ZnCl_2 \cdot C_4H_9O]H$ results in the production of ethyl acetate, the yield being 70-75% of the theoretical; when we condensed butyraldehyde with ethyl alcohol, using $[ZnCl_2 \cdot C_2H_5O]H$ or $[ZnCl_2 \cdot (C_5H_{11}O)_2]H2$, we secured butyraldehyde acetal, the yield being as high as 55% of the theoretical.

We also performed a few condensations of alcohols with aromatic compounds in the presence of $ZnCl_2$ at various temperatures in order to shed some light on the mechanism involved in alkylation with alcohols. We found that alkylation involves a stage in which olefins are formed, and that the temperature required for a successful reaction is somewhat higher than that required for the cleavage of the coordination compounds of $ZnCl_2$ and alcohols. The alkylation of toluene with n-butyl, n-propyl, and isoamyl alcohols, for example, does not take place at 165-175°, even when the quantity of $ZnCl_2$ used is substantial. When these reactions are carried out at high temperatures (200-220°), we get the respective alkyl derivatives. Alkylation with isopropyl alcohol occurs at 170-175° (the cleavage temperature is 160-165°). The fact that the alkylation reaction involves a stage in which olefins are produced is also borne out by the production of secondary alkyl derivatives with alcohols of normal structure employed [5].

We have also found that aromatic hydrocarbons (benzene, toluene) are not alkylated by olefins in the presence of $ZnCl_2$.

These findings lead us to believe that the various alkylations of aromatic compounds with alcohols, using $ZnCl_2$, involve a stage in which coordination compounds of the $[ZnCl_2 \cdot OR]H$ or $[ZnCl_2 \cdot (OR)_2]H_2$ type are produced, these compounds then breaking down into the respective olefins under the reaction conditions. Then the olefins condense with the aromatic hydrocarbons under the influence of the complex acids $[ZnCl_2 \cdot OH]H$ or $[ZnCl_2 \cdot OR]H$, yielding the respective alkyl derivatives:

$$R{-}CH_2{-}CH_2OH + ZnCl_2 \rightarrow [R{-}CH_2{-}CH_2O \cdot ZnCl_2]H, \quad (1)$$

$$[R{-}CH_2{-}CH_2O \cdot ZnCl_2]H \rightarrow R{-}CH{=}CH_2 + [ZnCl_2 \cdot OH]H, \quad (2)$$

$$R{-}CH{=}CH_2 + HAr \rightarrow Ar{-}CH\begin{matrix}CH_3\\ R\end{matrix}. \quad (3)$$

We have also found that molar compounds of $ZnCl_2$ with water possess catalytic properties. When benzene is alkylated or acylated in the presence of $[ZnCl_2 \cdot OH]H$, we get up to 30% of the respective products. Alkylating toluene with butyl chloride at 180-190° in the presence of $[ZnCl_2 \cdot OH]H$ results in the formation of a mixture of butyltoluenes, the yields being as high as 55%. To compare the catalytic activity of $ZnCl_2$ with that of other metal halides we performed several condensations of benzene with n-propyl and n-butyl alcohols. These reactions yielded no results with $CaCl_2$, $CdCl_2$, $MgCl_2$, or $BaCl_2$, even at 250-260°. This is due to the fact that the alcohols are driven off from alcoholic solutions of these metal chlorides at high temperatures, without any olefins being produced.

I wish to express my profound gratitude to Prof. I. P. Tsukervanik and Prof. V. V. Udovenko for their assistance and counsel.

EXPERIMENTAL

I. Coordination Compounds of Zinc Chloride and Alcohols

The zinc chloride was dehydrated by fusing a pure preparation with conc. HCl (sp. gr. 1.19). The alcohols were thoroughly dried by refluxing them for a long time with CaO and then fractionating; then they were dried again over anhydrous $CuSO_4$ and fractionated over Na. The reaction was performed in a flask connected to a reflux condenser, the mixture of reagents being heated for 4-5 hours. When the reaction was over, the mass was repeatedly treated with a mixture of diethyl and petroleum ethers. The resultant oily reaction products were analyzed after the excess solvent had been eliminated by evaporation in vacuo (15-20 mm at 45-50°).

1. Methanol-zinc chloride. We used 3.5 g of CH_3OH and 9.7162 g of $ZnCl_2$; when the reagents were mixed together, the mass warmed up considerably. The mixture was heated 5 hours at 150-155°. The excess alcohol was removed from the resultant oily product by evaporation in vacuo (15-20 mm) at 45-50° or without the use of vacuum

at 145-150° to constant weight. This yielded 12.1022 g of a product (9.7162 g theoretically). $ZnCl_2$ should combine with 2.286 g of CH_3OH, giving rise to 12.0022 g of $CH_3OH \cdot ZnCl_2$. The same product was obtained by treating the reaction mixture with a mixture of diethyl and petroleum ethers, followed by evaporating the excess solvent (15-20 mm at 45-50°).

The synthesized product is a bright, thick oil that possesses marked acidic properties. When the product is heated to 180°, it is cleaved, giving rise to dimethyl ether. Practically no unsaturated compounds are formed. Analysis for C, H, Zn, and Cl showed that its composition was that of $CH_3OH \cdot ZnCl_2$.

d_{40}^{40} 1.857; n_D^{20} 1.5105; MR_D 27.00; calculated 26.34.

0.0730 g substance: 43 ml 0.02 N. $AgNO_3$. 0.1888 g substance: 16.5 ml $K_4Fe(CN)_6$ (f = 0.766) and in back-titration 1.30 ml $ZnSO_4$ (f = 1.033). 0.150 g substance: 0.0374 g CO_2; 0.029 g H_2O. Found %: Cl 41.30; Zn 39.10; C 6.81; H 2.20. $CH_3OH \cdot ZnCl_2$. Calculated %: Cl 42.00; Zn 38.80; C 7.14; H 2.41.

2. Ethyl alcohol-zinc chloride. We used 9.2 g (0.2 mole) of C_2H_5OH and 6.541 g of $ZnCl_2$. Considerable heat was evolved when they were mixed together, the temperature of the mixture rising to 45°. The reaction mass was heated to 140-145° for 5 hours. When the reaction was over, the product was evaporated in vacuo (40-45°; 15-20 mm) to constant weight. This yielded 8.701 g of product. The substance was a bright oil with a peculiar odor. When it was heated to 170-175°, it was cleaved, yielding ethyl alcohol, acetaldehyde and ethylene.

d_{40}^{40} 1.800; n_D^{20} 1.5125; MR_D 30.36; calculated 30.96.

0.1090 g substance: 0.050 g CO_2; 0.0344 g H_2O. 0.1166 g substance: 64 ml $AgNO_3$. 0.2684 g substance: 21 ml $K_4Fe(CN)_6$. 1.20 ml $ZnSO_4$. Found %: C 12.51; H 3.55; Cl 38.14; Zn 36.14. $C_2H_5OH \cdot ZnCl_2$. Calculated %: C 13.18; H 3.31; Cl 38.89; Zn 35.36.

3. n-Propyl alcohol-zinc chloride. We used 18 g (0.3 mole) of n-C_3H_7OH and 34 g (0.25 mole) of $ZnCl_2$, and heated to 160-165° for 4 hours. After the reaction was over, the mass was processed with a mixture of ethers; evaporation in vacuo to constant weight to eliminate the solvent yielded a bright oil; it decomposed at 205-210°, giving rise to propylene.

d_{40}^{40} 1.630; n_D^{20} 1.5193; MR_D 36.48; calculated 35.57.

0.0548 g substance: 28.90 ml $AgNO_3$. 0.2188 g substance: 16 ml $K_4Fe(CN)_6$. 2.10 ml $ZnSO_4$. Found %: Cl 36.64; Zn 33.16. $C_3H_7OH \cdot ZnCl_2$. Calculated %: Cl 36.20; Zn 33.40.

4. Isopropyl alcohol-zinc chloride. We used 9 g (0.15 mole) of C_3H_7OH and 10 g of $ZnCl_2$. Heating to 130-140° for 4 hours. This yielded a bright oil, which decomposed at 150-160°, producing propylene.

d_{40}^{40} 1.589; n_D^{20} 1.4908; MR_D 35.98; calculated 35.57.

0.051 g substance: 26.80 ml $AgNO_3$. 0.2458 g substance: 17.50 $K_4Fe(CN)_6$, 0.7 ml $ZnSO_4$. Found %: Cl 36.88; Zn 33.75. $C_3H_7OH \cdot ZnCl_2$. Calculated %: Cl 36.20; Zn 33.40.

5. Normal butyl alcohol-zinc chloride. We used 15.0 g (0.2 mole) of C_4H_9OH and 14 g (0.1 mole) of $ZnCl_2$, and heated to 160-165° for 5 hours. This yielded a thick oil, which decomposed at 175-185°, producing butylene.

d_{40}^{40} 1.539; n_D^{20} 1.4910; MR_D 40.18; calculated 39.70.

0.0454 g substance: 21.60 ml $AgNO_3$. 0.1314 g substance: 11.00 ml $K_4Fe(CN)_6$, 2.00 ml $ZnSO_4$. Found %: Cl 33.06; Zn 31.64. $C_4H_9OH \cdot ZnCl_2$. Calculated %: Cl 33.76; Zn 31.10.

6. Isobutyl alcohol-zinc chloride. We used 15 g (0.2 mole) of C_4H_9OH and 14 g (0.1 mole) of $ZnCl_2$, and heated to 140-150° for 5 hours. This yielded an oil.

d_{40}^{20} 1.550; n_D^{20} 1.490; MR_D 39.00; calculated 39.70:

0.0474 g substance: 23 ml $AgNO_3$. 0.1416 g substance: 11.00 ml $K_4Fe(CN)_6$, 1.70 ml $ZnSO_4$. Found %: Cl 33.72; Zn 30.79. $C_4H_9OH \cdot ZnCl_2$. Calculated %: Cl 33.76; Zn 31.10.

7. Ethylene glycol-zinc chloride. We used 12.5 g (0.2 mole) of ethylene glycol and 14 g of $ZnCl_2$. Heating to 150-155° for 6 hours. This yielded a transparent, thick oil.

d_{40}^{40} 1.7950; n_D^{20} 1.5168; MR_D 33.50; calculated 32.73.

0.0550 g substance: 27.30 ml $AgNO_3$. 0.2376 g substance: 17.00 ml $K_4Fe(CN)_6$, 1.40 ml $ZnSO_4$. Found %: Cl 34.50; Zn 31.91. $C_2H_5O_2 \cdot ZnCl_2$. Calculated %: Cl 35.25; Zn 32.46.

8. Cyclohexanol-zinc chloride. We used 10 g (0.1 mole) of $C_6H_{12}O$ and 12 g of $ZnCl_2$. Heating to 120-125° for 10 hours. When the reaction mass was allowed to stand for several days, crystals settled out, which were quickly filtered and washed with petroleum ether. This yielded white needles with an m.p. of 80-82°. To judge by the results of analysis, the resultant substance has the composition of $(C_6H_{12}O)_2 \cdot ZnCl_2$. It is acidic and hygroscopic. When heated to 140°, it is cleaved into cyclohexene (b.p. 82-84°) and a product with a b.p. of 230-240° (whose composition was not determined).

0.0456 g substance: 14.00 ml $AgNO_3$. 0.0774 g substance: 5.70 ml $K_4Fe(CN)_6$, 2.00 ml $ZnSO_4$. 0.1024 g substance: 0.1591 g CO_2; 0.0630 g H_2O. Found %: Cl 21.33; Zn 19.90; C 42.41; H 6.83. $(C_6H_{12}O)_2 \cdot ZnCl_2$. Calculated %: Cl 21.10; Zn 19.48; C 42.85; H 7.14.

II. Alkylation, Acylation and Esterification with Coordination Compounds of Zinc Chloride.

1. Synthesis of ethyl acetate. We used 40 g of CH_3COOH (glacial), 40 g of C_2H_5OH and 20 ml of $[C_2H_5O \cdot ZnCl_2]H$. The reaction was carried out in a round-bottomed flask connected to a straight condenser. The catalyst was heated to 130-140° and then a mixture of the acetic acid and the alcohol was slowly added from a dropping funnel. Appropriate processing of the reaction product yielded 45 g (73%) of ethyl acetate (b.p. 76-78°; d_{20}^{20} 0.898).

Similar results were secured when the reaction was carried out with $[C_6H_5O \cdot ZnCl_2]H$.

2. Synthesis of an acetal from butyraldehyde and ethyl alcohol. We used 14.5 g of C_4H_8O, 30 g of C_2H_5OH, and 4 ml of $[C_2H_5O \cdot ZnCl_2]H$. The mixture warmed up considerably when the reagents were mixed together. The reaction mass was allowed to stand at room temperature for 48 hours. Then it was heated to 70-80° (water bath) for another 12 hours. Appropriate processing of the reaction products yielded 15 g of the acetal (52%), with a b.p. of 141-142° (725 mm); d_{20}^{20} 0.8410 [7].

3. Condensation of toluene with trimethylethylene. We used 25 ml of C_7H_8, 10 ml of trimethylethylene (b.p. 36-38°), and 10 ml of $[C_2H_5O \cdot ZnCl_2]H$, heating it to 200-205° in a bomb for 10 hours. This yielded 4 g (25%) of a mixture of tertiary amyltoluenes plus some diamylene. We isolated p-tert-amyltoluene [8], b.p. 204-206° (725 mm); d_{20}^{20} 0.8654, n_D^{20} 1.4945. The b.p. of the diamylene was 152-154°.

4. Condensation of benzene with n-butyl chloride. We used 27 ml of C_6H_6, 9.2 ml (0.1 mole) of C_4H_9Cl, and 4 ml of $[C_2H_5O \cdot ZnCl_2]H$. The reagent mixture was heated to 80-85° for 10 hours, with vigorous stirring, in a round-bottomed flask connected to a reflux condenser. This yielded 3 g (22.5%) of butylbenzene. Fractionation of the crude product yielded sec-butylbenzene [9]:

B.p. 170-172°; d_{20}^{20} 0.8625; n_D^{20} 1.4915; MR_D 45.56; calculated 45.70.

The results were negative when the reaction was carried out under similar conditions with $ZnCl_2$, $CdCl_2$, or $MgCl_2$ present. Performing the reaction at 180-190° in the presence of $[ZnCl_2 \cdot OH]H$ resulted in the formation butyltoluenes, the yields being as high as 55%.

5. Condensation of toluene with benzoyl chloride. We used 14 g (0.2 mole) of C_6H_5COCl, 20 ml of C_7H_8, and 4 ml of $[C_2H_5O \cdot ZnCl_2]H$. When the catalyst was added to a mixture of toluene and benzoyl chloride, the mass warmed up considerably, HCl being evolved. Then the reagent mixture was refluxed at 75-80°, with stirring, for 8 hours from a round-bottomed flask. This yielded 5 g (25.5%) of 4-methylbenzophenone [9]; crystals with an m.p. of 53-54°; oxime m.p. 153-154°.

Negative results were obtained when this reaction was performed under similar conditions with $ZnCl_2$ present. When the reaction was carried out with the crystalline substance with the composition of $(C_6H_{12}O)_2 \cdot ZnCl_2$, we again secured 4-methylbenzophenone. The use of concentrated alcoholic solutions of $CaCl_2$ as a catalyst did not yield the desired results.

SUMMARY

1. Molecular compounds of methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, and isoamyl alcohols and of ethylene glycol with $ZnCl_2$ have been prepared. The compositions of these compounds correspond to the formula $ROH \cdot ZnCl_2$; cyclohexanol yields a compound of the $(C_6H_{12}O)_2 \cdot ZnCl_2$ type.

2. A study of the properties of the synthesized molecular compounds of $ZnCl_2$ with alcohols has served to indicate the mechanism of alkylation with $ZnCl_2$; the catalytic properties of molecular compounds of $ZnCl_2$ have been studied.

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PHYSICOCHEMICAL RESEARCH ON THE REACTION OF TITANIUM TETRACHLORIDE WITH ISOAMYL ACETATE

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The researches of N. S. Kurnakov and his associates [1, 2], on the systems produced by stannic chloride and bromide with esters of monobasic acids point to the existence in the liquid phase of compounds of the general type: $SnHal_4 \cdot 2E$, where E denotes a molecule of an ester of a monobasic acid.

As the molecular weight of the acid is raised, the heat evolved in the reaction of stannic chloride with the ester drops, which is reflected in the nature of the viscosity diagram.

We were interested in making a study of the behavior of titanium chloride with esters of monobasic acids and comparing the results obtained with the findings for stannic chloride. The present paper sets forth the results of an investigation of the viscosity, density, and conductance of the system formed by titanium chloride and isoamyl acetate.

Reagents and experimental procedure. The titanium chloride (c.p.) was not especially purified and was stored in sealed test tubes. The isoamyl acetate was dried for a long time over calcium chloride and then distilled, the fraction boiling at 142-143°; d_4^{17} 0.8752; n_D^{17} 1.4014 being used in our research. In every instance the solution concentration is expressed in molar per cent.

Since considerable heat was evolved when the components were mixed, the solutions were prepared in double-elbow vessels with ground-glass stoppers. Each component was poured into a separate elbow, after which they were gradually mixed together with constant chilling. Only when the foregoing precautions were taken could we prevent an explosion and obtain transparent mixtures.

The solutions were kept for a few hours at a temperature 5-10° above the melting point of the resultant solid products, in order to complete the reaction and secure equilibrium systems.

Viscosity was measured in a viscosimeter of the closed type. To prevent the entrance of moisture during the filling of the viscosimeter bulb, the latter was connected by rubber tubing and a threeway stopcock to one of two communicating vessels, which contained mercury, the level of which changed as the other vessel was raised or lowered, thus producing the rarefaction required to draw the solution into the bulb of the viscosimeter.

Conductance was measured by Kohlrausch method. Current was supplied by an audio-frequency generator, with a drum bridge serving as the slide wire. A vessel with a tightly fitting polished cover was used in the measurements.

Density was measured in a 5-8 ml pyknometer. The temperature of the liquid under test was kept constant within $\pm 0.1°$ by means of an oil thermostat.

The density, viscosity, and conductance were measured at 60° and 70°. These temperature limits were fixed, on the one hand, by the fairly rapid formation of crystals below 60° and by the circumstance, on the other hand, that the melt began to resinify partially at any temperature above 70°.

Results of measurement. The figures for the viscosity of the system are given in Table 1 and Fig. 1. As we see, the viscosity isotherms all pass through distinct maxima, corresponding to equimolar proportions of the components. Hence, a compound with the composition of $TiCl_4 \cdot CH_3COOC_5H_{11}$ is formed within the system. The viscosity isotherms indicate that our system approaches a rational one.

At 60° the viscosity at the maximum is 72.5 times as great as that of the more viscous component. The

TABLE 1

Viscosity of the Titanium Chloride – Isoamyl Acetate System

Solution No.	Mol. % of $TiCl_4$	Viscosity, centipoises 60°	70°	Relative temperature coefficient
1	0.00	0.54	0.49	0.97
2	15.30	1.38	1.18	1.56
3	31.30	10.0	7.87	3.32
4	40.00	22.05	15.10	3.74
5	45.30	35.50	18.82	6.14
6	49.90	44.23	21.13	7.08
7	55.40	21.29	11.41	6.04
8	60.00	11.50	6.88	5.05
9	63.70	7.16	4.62	4.31
10	81.40	1.37	1.22	1.16
11	100.00	0.61	0.57	0.68

viscosity isotherms diverge widely in the region close to the 1:1 component ratio, which is evidence of the high temperature coefficient of viscosity at these concentrations.

We calculated the relative temperature coefficient from the following formula:

$$\gamma = \frac{1}{\frac{\eta_1 + \eta_2}{2}} \cdot \frac{\eta_1 - \eta_2}{t_2^\circ - t_1^\circ},$$

where η_1 and η_2 are the numerical values of the viscosity at the temperatures t_1° and t_2°.

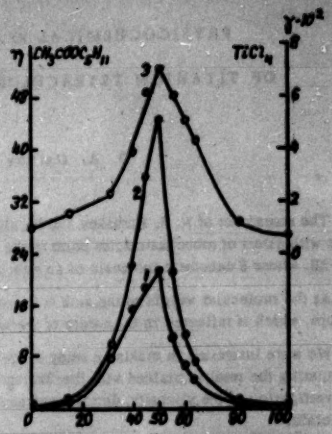

Fig. 1.
Viscosity of the titanium chloride–isoamyl acetate system and its temperature coefficient. 1) η_{70°; 2) η_{60°; 3) γ_{60-70°.

The curve of the relative temperature coefficient reproduced in the upper part of Fig. 1, has a shape that resembles that of the viscosity isotherms themselves, i.e., it passes through a distinct maximum, corresponding to the formation of a chemical compound within the system.

TABLE 2

Density of the Titanium Chloride – Isoamyl Acetate System

Solution No.	Mol. % of $TiCl_4$	Density 60°	70°
1	0.00	0.8330	0.8221
2	15.30	0.9872	0.9764
3	31.30	1.1769	1.1678
4	40.00	1.2650	1.2450
5	45.30	1.3215	1.3022
6	49.90	1.3654	1.3429
7	55.40	1.4020	1.3822
8	60.00	1.4282	1.4006
9	63.70	1.4490	1.4313
10	81.40	1.5456	1.5320
11	100.00	1.6528	1.6339

The density is given as a function of the composition in Table 2 and represented graphically in Fig. 2. The density isotherms of the system consist of two nearly linear branches, which meet at a point that represented 50 mol. % of each component. Such a shape of the isotherm of this property, which is usually much less distinct, is evidence of pronounced chemical action between the titanium chloride and the isoamyl acetate. The positive declination of the density isotherms from the additive straight lines for the 50 mol. % solution was 9.8% at 60° and 9.4% at 70°.

The results of our measurements of the system's conductance are given in Table 3, and Fig. 3.

The conductance isotherms exhibit two maxima and a distinct minimum, occurring at 50 mol. % of titanium chloride. In conformity with the M. A. Klochko classification [3], the isotherm of this system should be assigned to the VIIth type of conductance diagrams. The fifth column of Table 3 gives the results of our calculations of the relative temperature coefficient of conductance, these figures being used in plotting the curve (top curve in Fig. 3), which passes through a maximum at the composition of the compound. If we eliminate the effect of viscosity upon conductance by the simplest formula, $\chi_{corr.} = \chi \cdot \eta$, we get the figures given in the last column of Table 3 and in Fig. 3. As we see, the curve of the derived conductance also exhibits a maximum, evidence of pronounced chemical action between the components.

The data we secured in our investigations of the viscosity, density, and conductance of the titanium

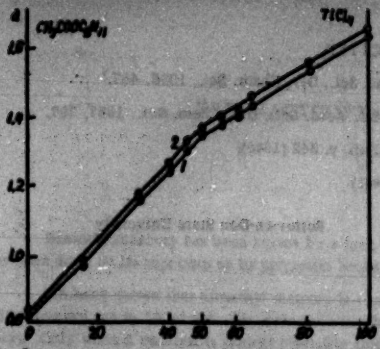

Fig. 2.
Density of the Titanium chloride—isoamyl acetate system 1) $d_{70}°$; 2) $d_{60}°$.

chloride-isoamyl acetate system lead us to conclude that the compound $TiCl_4 \cdot CH_3COOC_5H_{11}$ is formed within the system, a compound that is hardly dissociated at all in the liquid phase. Hence, we may say that our system is close to a rational one as far as interaction is concerned.

As our experimental data indicate, titanium chloride forms a molecular compound with only one molecule of isoamyl acetate, but not with two molecules as is the case with stannic chloride. We assume that this fact may be attributed to steric hindrances, since the tetrahedral covalent radius of Ti^{IV} (1.28 Å) is smaller than that of Sn^{IV} (1.40 Å). This steric hindrance apparently gives rise to the comparatively large radical C_5H_{11}.

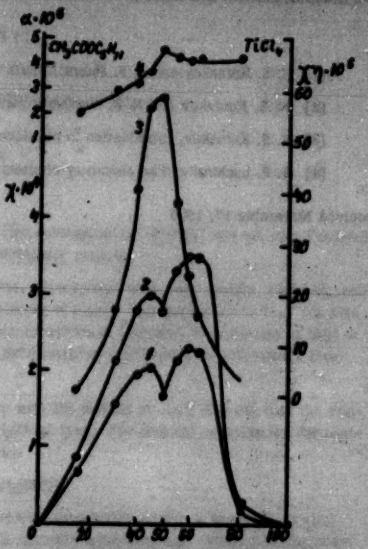

Fig. 3. Specific conductance of the titanium chloride—isoamyl acetate system, its temperature coefficient, and its derived conductance.
1) $\chi_{60}°$; 2) $\chi_{70}°$; 3) χ_{π}; 4) $\alpha_{70}-\alpha°$.

TABLE 3
Conductance of the Titanium Chloride–Isoamyl Acetate System

Solution No.	Mol. % of $TiCl_4$	Specific conductance, $\chi \cdot 10^4$		Relative temperature coefficient, $\alpha \cdot 10^6$	Derived conductance, $\chi_{70}° \cdot \eta_{70}° \cdot 10^6$
		60°	70°		
1	0.00	0.00	0.00	–	–
2	15.30	0.70	0.83	2.12	1.03
3	31.30	1.57	2.13	3.03	16.76
4	40.0	1.95	2.72	3.30	41.10
5	45.30	2.03	2.99	3.82	56.28
6	49.90	1.67	2.77	4.96	58.53
7	55.40	2.14	3.33	4.35	37.99
8	60.0	2.30	3.51	4.25	24.15
9	63.70	2.25	3.47	4.27	16.03
10	81.40	0.18	0.28	4.30	0.34
11	100.00	0.00	0.00	–	–

As a matter of fact, two types of compounds: $TiCl_4 \cdot (C_5H_{11})_2O$ and $TiCl_4 \cdot 2(C_5H_{11})_2O$, are known [4] for ethers.

It is highly likely that titanium chloride, like $SnCl_4$, forms molecular compounds of the $TiCl_4 \cdot 2E$ type with esters of monobasic acids and the simplest alcohols.

SUMMARY

1. The viscosity, density, and conductance of the titanium chloride–isoamyl acetate system have been studied at 60 and 70°.

2. It has been shown that a compound, $TiCl_4 \cdot CH_3COOC_5H_{11}$, which is hardly dissociated at all in the liquid phase, is formed in the system.

3. The relative temperature coefficients of viscosity and conductance and the derived conductance have been computed.

4. An attempt is made to explain the formation of a compound with equimolar proportions of the components titanium chloride and isoamyl acetate.

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THE REACTIVITY OF DIMETHYLMERCURY

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Dimethylmercury has been known for a long time; it was first synthesized in 1858 [1], but not much research has been done on its reactions or its properties because of its extraordinary toxicity.

We have shown that dimethyl mercury is a stable compound, decomposing only very slightly, yielding metallic mercury (up to 1% of metallic mercury) when heated in a solution of alcohol and pyrogallol to 130° for 6-10 hours. Only when a catalyst is present (metallic gold) does the decomposition of dimethyl mercury rise as high as 10% after 10 hours of heating to 130°. Diphenylmercury and dinaphthylmercury decompose 75-100% under these same conditions [2].

We then made a study of the reactions of dimethylmercury with the phenols at 130°, showing that the principal products were monomercurated derivatives of the $CH_3HgC_6H_3(OH)R$ type. The general equation for the reaction of dimethylmercury with the phenols may be written as follows:

$$(CH_3)_2Hg + RC_6H_4OH \rightarrow CH_4 + CH_3HgC_6H_3(OH)R.$$

Resorcinol produced dimercurated derivatives when reacted with dimethylmercury. Pronounced tarring occurs with pyrogallol, pyrocatechinol, and hydroquinone, metallic mercury separating out. When dimethylmercury is reacted with organic acids at 130°, we get colorless crystalline substances, with the general formula of $RCOOHgCH_3$, methane being evolved in accordance with the following equation:

$$(CH_3)_2Hg + RCOOH \rightarrow CH_4 + RCOOHgCH_3.$$

Dimethylmercury reacts with phthalic acid to form a dimercurated derivative $C_6H_4(COOHgCH_3)_2$.

EXPERIMENTAL

I. Synthesis of dimethylmercury. The dimethylmercury was prepared by the Wilde method [3] as follows: 7.5 kg of 0.4% sodium amalgam was placed in a tubular thick-walled flask, and a mixture of 80.0 g of methyl iodide and 10.0 g of ethyl acetate was poured in through an externally chilled reflux condenser, an energetic reaction taking place. The next day water was added, and the liquid was separated from the mercury, thoroughly washed with water, an alkali solution, and again with water, dried and fractionated. The dimethylmercury yield is 60%. The dimethylmercury had a b.p. of 91-93° and a d 3.064.

0.0892 g substance: 7.74 ml 0.1 N NH_4CNS. Found %: Hg 86.77. $(CH_3)_2Hg$. Calculated %: Hg 87.00.

All the experiments made in our investigation of the reactivity of dimethylmercury were performed by heating a mixture of the reagents in sealed glass ampoules in a thermostat equipped with precise temperature control.

II. Reaction of dimethylmercury with phenols. In every instance the ampoules were opened with an explosion after the reagent mixture was heated to 130° for 3 hours, a combustible gas (methane) being evolved.

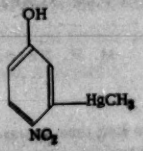
1) Dimethylmercury and p-nitrophenol. 0.3 gram of p-nitrophenol was used for 0.5 g of dimethylmercury. The reaction mass was yellow in color. Processing with alcohol yielded 0.35 g of yellow acicular crystals with an m.p. of 169-170°.

0.0588 g substance: 3.32 ml 0.1 N NH_4CNS. Found %: Hg 56.46. $CH_3HgC_6H_3(OH)NO_2$. Calculated %: Hg 56.62.

The synthesized compound is readily cleaved by an alcoholic solution of HCl; at -10° it forms p-nitrophenol and methylmercury chloride with an m.p. of 169-170° (mixed melting point 170°). The m.p. of the p-nitrophenol was 112-113° after recrystallization, its mixed melting point being 113-114° (the literature cites 114°).

Processing the synthesized compound with a solution of bromine in potassium bromide cleaved it, yielding 3-bromo-4-nitrophenol, with an m.p. of 128-129° (the literature cites 129-130° [4]).

The synthesized monomercurated derivative of dimethylmercury and p-nitrophenol is, therefore, 3-methylmercury-4-nitro-1-hydroxybenzene:



2) Dimethylmercury and o-nitrophenol. No reaction took place within 3 hours at 130°.

3) Dimethylmercury and 2,4,6-trinitrophenol. 0.6 gram of trinitrophenol used for 0.5 g of dimethylmercury. The reaction mass yielded 0.42 g of yellow acicular crystals, with an m.p. of 125-127°, freely soluble in alcohol and in ether.

0.0860 g substance: 3.89 ml 0.1 N NH_4CNS. Found %: Hg 45.23. $CH_3HgC_6H(OH)(NO_2)_2$. Calculated %: Hg 45.40.

4) Dimethylmercury and 2,4-dichlorophenol. 0.3 gram of dichlorophenol used for 0.5 g of dimethylmercury. The reaction mass was white. Recrystallization from alcohol yielded 0.4 g of white acicular crystals with an m.p. of 123-125°.

0.0520 g substance: 11.10 ml 0.05 N $Na_2S_2O_3$. Found %: Hg 53.36. $CH_3HgC_6H_2(OH)Cl_2$. Calculated %: Hg 53.12.

5) Dimethylmercury and 2,4,6-trichlorophenol. 0.4 gram of trichlorophenol was used for 0.5 g of dimethylmercury. The reaction mass was white. Recrystallization from alcohol yielded 0.38 g of white acicular crystals with an m.p. of 120°.

0.0494 g substance: 9.52 ml 0.05 N $Na_2S_2O_3$. Found %: Hg 48.18. $CH_3HgC_6H(OH)Cl_3$. Calculated %: Hg 48.68.

The compound is readily cleaved by the action of an alcoholic solution of HCl, yielding methylmercury chloride with an m.p. of 169-170° and 2,4,6-trichlorophenol with an m.p. of 66-67°, its mixed melting point being 67°.

6) Dimethylmercury and resorcinol. 0.25 gram of resorcinol was used for 0.5 g of dimethylmercury. The reaction mass was red. Processing with organic solvents left as a residue a pink crystalline powder (0.35 g) with an m.p. of 200-202° with decomposition.

0.0546 g substance: 4.05 ml 0.1 N NH_4CNS. Found %: Hg 74.17 $(CH_3Hg)_2C_6H_2(OH)_2$. Calculated %: Hg 74.27.

III. Reaction of dimethylmercury with organic acids. In every instance the reagent mixture was heated to 130° for 3 hours, after which the ampoules were opened, an explosion taking place, and a combustible gas being given off (methane). 0.0025 mole of acid was used per 0.003 mole of dimethylmercury.

1) Dimethylmercury and acetic acid. A transparent liquid, which forms a transparent oil at the bottom of the vessel when poured into water, the oil slowly crystallizing upon standing. White acicular crystals with an m.p. of 126-128°. The yield was 40% of the theoretical.

0.0812 g substance: 5.90 ml 0.1 N NH_4CNS. Found %: Hg 72.66. $CH_3COOHgCH_3$. Calculated %: Hg 72.72.

2) Dimethylmercury and propionic acid. A transparent liquid that slowly crystallized when poured into water. White crystals with an m.p. of 67-68°. 40% of the theoretical yield.

0.0554 g substance: 3.84 ml 0.1 N NH_4CNS. Found %: Hg 69.31. $C_2H_5COOHgCH_3$. Calculated %: Hg 69.50.

3) Dimethylmercury and isovaleric acid. A transparent liquid that slowly crystallized when poured into water. White acicular crystals with an m.p. of 58-59°. 33% of the theoretical yield.

0.0954 g substance: 5.99 ml 0.1 N NH_4CNS. Found %: Hg 62.78. $C_4H_9COOHgCH_3$. Calculated %: Hg 63.86.

4) Dimethylmercury and stearic acid. A white crystalline mass that dissolves readily in organic solvents. Recrystallization from benzene and then from alcohol yielded crystals with an m.p. of 80-81°. 72% of the theoretical yield.

0.0566 g substance: 2.27 ml. 0.1 N NH_4CNS. Found %: Hg 40.10. $C_{17}H_{35}COOHgCH_3$. Calculated %: Hg 40.23.

5) Dimethylmercury and benzoic acid. A white crystalline mass. Recrystallization from alcohol yielded crystals with an m.p. of 106-107°. 60% of the theoretical yield.

0.1060 g substance: 6.29 ml. 0.1 N NH_4CNS. Found %: Hg 59.34. $C_6H_5COOHgCH_3$. Calculated %: Hg 59.59.

6) Dimethylmercury and salicylic acid. White crystalline mass. Recrystallization from alcohol yielded crystals with an m.p. of 113-114°. 70% of the theoretical yield.

0.1120 g substance: 6.34 ml 0.1 N. NH_4CNS. Found %: Hg 56.60. $C_6H_4(OH)COOHgCH_3$. Calculated %: Hg 56.89.

7) Dimethylmercury and phthalic acid. White crystalline mass. Recrystallization from alcohol yielded crystals with an m.p. of 223-224° with decomposition.

0.1024 g substance: 6.88 ml 0.1 N NH_4CNS. Found %: Hg 67.18. $C_6H_4(COOHgCH_3)_2$. Calculated %: Hg 67.40.

IV. Decomposition of dimethylmercury. Experiment 1. Dimethylmercury (0.3 g), pyrogallol (0.2 g), alcohol (3 ml), 130°, 6 hours. 1.1% of metallic mercury was found after heating was over.

Experiment 2. Dimethylmercury (0.3 g), alcohol (3 ml), 150°, 6 hours. No decomposition.

Experiment 3. Dimethylmercury (0.3 g), gold (0.2 g), alcohol (3 ml), 130°, 10 hours. 10.1% of metallic mercury was found after heating was over.

SUMMARY

1. When dimethylmercury is reacted with phenols, the principal products are monomercurated derviatives with the following general formula: $CH_3HgC_6H_3(OH)R$.

2. When dimethylmercury is reacted with organic acids, crystalline compounds with the following general formula, $RCOOHgCH_3$, are produced.

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THE REACTION OF DIPHENYLMERCURY WITH ESTERS

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In the study of the reactivity of organometallic compounds no work at all has been done on their reaction with esters. In the course of our systematic investigation of the reactions of aromatic compounds of mercury and other metals, we made a study of the reaction of diphenylmercury with 12 esters. We found that diphenylmercury reacts with esters when heated to 150° for 6-9 hours, giving rise to derivatives whose general formula is $RCOOHgC_6H_5$. Thus, the reaction of diphenylmercury with methyl acetate yields toluene and phenylmercury acetate, as follows:

$$(C_6H_5)_2Hg + CH_3COOCH_3 \rightarrow C_6H_5CH_3 + C_6H_5HgOCOCH_3.$$

When diphenylmercury is reacted with propyl and butyl formate, a high percentage of metallic mercury (65-68%) is evolved, due to the decomposition of the phenylmercury formate produced during the reaction. [1] Metallic mercury is precipitated and $RCOOHgC_6H_5$ is produced when diphenylmercury is reacted with ethyl acetate, butyl butyrate, and benzyl benzoate.

It should be said that butyrates react most readily with diphenylmercury, while of the other RCOOR' esters, those that have a methyl group as the R' radical are most reactive.

When we compare the reaction of diphenylmercury with esters and organic acids, we see that although diphenylmercury reacts very easily and smoothly (at 100°) with organic acids, producing a quantitative yield of $RCOOHgC_6H_5$, the reaction of diphenylmercury with esters is much harder (at 150°), metallic mercury being produced in several instances alongside the $RCOOHgC_6H_5$.

EXPERIMENTAL

All our experiments were performed by heating a mixture of the reagents in sealed glass ampoules immersed in a thermostat provided with accurate temperature regulation. 1.5 ml of the ester was used for 0.5 g of the diphenylmercury. The temperature was 150°, and the run lasted 6 hours (see table).

1. Diphenylmercury and methyl acetate. 9 ml of methyl acetate to 2.0 g of diphenylmercury, 150°, 9 hours. Toluene was formed, together with 1.08 g of a crystalline precipitate of phenyl-mercury acetate with an m.p. of 146-148°.

0.1118 g substance: 6.72 ml 0.1 N NH_4CNS. Found %: Hg 60.11. $C_6H_5HgOCOCH_3$. Calculated %: Hg 59.60.

2. Diphenylmercury and propyl butyrate. 3 ml of propyl butyrate to 1.0 g of diphenylmercury, 150°, 9 hours.

This yielded 0.5 g of phenylmercury butyrate with an m.p. of 90-92° (91° given in the literature).

0.05 g substance: 2.74 ml 0.1 N NH_4CNS. Found %: Hg 54.80. $C_6H_5HgOCOC_3H_7$. Calculated %: Hg 55.02.

Processing with alcoholic HCl yielded butyric acid and phenylmercury chloride with an m.p. of 250-251° (mixed melting point: 250°).

SUMMARY

1. A study has been made of the reaction between diphenylmercury and esters.

2. It has been shown that at 150° diphenylmercury enters into reaction with esters, giving rise to the respective derivatives whose formulas are $RCOOHgC_6H_5$.

3. In some instances metallic mercury is precipitated in addition to the formation of the $RCOOHgC_6H_5$ compounds.

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REACTION OF DIPHENYLMERCURY WITH ESTERS

No.	Ester	Quantity $C_6H_5HgOCOR$ produced		% metallic mercury precipitated	Remarks
		Grams	Per cent		
1	Methyl acetate	0.22	46.3	0	
2	Ethyl acetate	0.10	21.8	11.3	
3	Propyl acetate	0	0	0	The diphenylmercury did not react
4	Butyl acetate	0	0	0	Ditto
5	Ethyl benzoate	0	0	0	Ditto
6	Benzyl benzoate	0	0	1.4	Tar
7	Propyl formate	0	0	64.9	
8	Butyl formate	0	0	68.3	
9	Methyl butyrate	0.27	52.5	–	
10	Ethyl butyrate	0.15	29.2	–	
11	Butyl butyrate	0.20	38.9	6.9	

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RESEARCH ON THE COMPARATIVE HYDROGENATION AND OXIDATION OF OCTADECENIC ACIDS

G. V. Pigulevsky and P. A. Artamonov

In our preceding report [1] we pointed out that the hydrogenation rate depends upon the position of the double bond in the chain. Octadecen-6-acid-1 is hydrogenated most slowly. Hydrogenation is speeded up as the double bond is shifted, the highest rate of hydrogenation being displayed by octadecen-9-acid-1 (oleic acid).

In the present research we have dealt with the problem of the influence of cis-trans isomerism upon the hydrogenation rate, then turning to examination of the comparative oxidation of octadecenic acids by benzoyl hydrogen peroxide.

Comparative hydrogenation of petroselinic acid (cis-octadecen-6-acid-1) and petroselaidic acid (trans-octadecen-6-acid-1). It is stated in the literature that the cis form is hydrogenated more rapidly than the trans form. This is especially true of oleic and elaidic acids [5]. Later research (Plisov and Golendeev [2]) on esters of oleic and elaidic acids yielded similar results. These findings together with X-ray and spectroscopic investigations [3] settled the question of the cis form of oleic acid. We still have no spectroscopic research results on petroselinic or petroselaidic acid. Our conviction that petroselinic acid has the cis form is not supported by enough experimental evidence. A comparative study of the rates of hydrogenation of these acids should clear up this problem.

Our research was done with petroselinic acid, secured from oil of coriander. The acid had an m.p. of 33°, an iodine number of 87.9, an n_D^{20} of 1.4415, and a neutralization number of 198.5. The petroselaidic acid was prepared by treating the lead salt of petroselinic acid with 10% nitric acid. The acid had an m.p. of 53°, an iodine number of 87.3, an n_D^{20} of 1.4395 and a neutralization number of 197.9.

The comparative hydrogenation conditions were the same as those used in the preceding paper. Hydrogenation was carried out simultaneously in the same agitation apparatus. The catalyst used was Willstatter platinum black. 1 gram of the acid, 30 ml of the solvent and 0.1 g of platinum black were placed in the "duck". We ran the tests with various solvents in order to secure clear results.

The first experiment was run with diethyl ether as a solvent. The hydrogenation results are given in Table 1. The figures cited (Table 1) indicate that petroselinic acid is hydrogenated more rapidly than the trans form, though the difference in the oxidation rates is slight. The hydrogenation reaction is not a first-order equation. The acid constant computed from this equation rises uninterruptedly. The results secured when hydrogenation was performed in chloroform were similar (Table 2). The results of our research on the hydrogenation of petroselinic and petroselaidic acids enable us to reach a conclusion concerning the cis form of petroselinic acid.

Comparative oxidation of octadecenic acids by benzoyl hydrogen peroxide. Prilezhaev has pointed out [4] that ability to undergo oxidation is governed by the structure of the organic compounds. For example, linanool, a tertiary alcohol with two isolated double bonds, can yield a monooxide and dioxide. Introducing an acetyl group changes the oxidizability of the molecule. Oxidation must be continued for two months to oxidize linalyl acetate.

This problem has been dealt with by Boeseken and his associates and by Meerwein. They found that such groups as $COOH$, C_6H_5, CN, NO_2, and CO retard the oxidation rate when they are located in the proximity of the double bond. In our research our objective was shedding light on the influence of the double bond in octadecenic acids upon the oxidation rate. The experiments were performed with $\Delta^{2,3}$-, cis-$\Delta^{6,7}$-, trans-$\Delta^{6,7}$-, and cis-$\Delta^{9,10}$ octadecenic acids. Oxidation was carried out under identical conditions in order to secure comparable results. Diethyl ether was used as the solvent. We used 0.5 g of the acid and an equimolar quantity of benzoyl hydrogen peroxide in every test. The acid concentration in the ether was 0.02975 mole per liter. The oxidation reaction kinetics were checked by determining the unreacted active oxygen left in the reaction mixture. The temperature fluctuated

TABLE 1 [1]

Comparative Hydrogenation in Diethyl Ether

Petroselinic acid				Petroselaidic acid			
t	v	Δv	k	t	v	Δv	k
5	28.0	23.0	5.60	5	26.0	21.5	5.20
10	51.0	17.1	4.60	10	47.5	16.3	4.30
15	68.1	16.9	3.42	15	63.8	16.4	3.26
20	85		3.38	20	89.2		3.28

TABLE 2

Comparative Hydrogenation in Chloroform

Petroselinic acid				Petroselaidic acid			
t	v	Δv	k	t	v	Δv	k
5	25.9	20.5	5.18	5	24.0	20.0	4.8
10	46.4	15.8	4.1	10	44.0	15.0	4.0
15	62.2	16.0	3.16	15	59.0	15.3	3.0
20	78.2		3.2	20	74.3		3.06

TABLE 3

Comparative Oxidation of Octadecenic Acids

t	$\Delta^{9,10}$		cis-$\Delta^{6,7}$		trans-$\Delta^{6,7}$		cis-$\Delta^{9,10}$	
	a-x	K	a-x	K	a-x	K	a-x	K
0	0.02975	–	–	–	–	–	–	–
60	0.02806	0.033	0.02606	0.078	–	–	0.02575	0.087
240	0.02409	0.033	0.01939	0.074	0.02108	0.057	0.01955	0.073
360	0.02338	0.025	0.01635	0.076	0.01934	0.052	0.01631	0.077
480	0.02292	0.021	0.01513	0.067	0.01748	0.049	0.01513	0.067
1147	0.02252	0.009	0.00924	0.065	0.01247	0.040	0.00923	0.065
1927	0.02100	0.007	0.00598	0.069	0.00949	0.037	0.00598	0.069

between 22.5 and 24° during the test. The constant K was calculated in conformity with a second-order equation. The time was given in minutes. The results of this comparative oxidation are given in Table 3.

As the double bond recedes from the carboxyl group, its effect upon the oxidation rate diminishes. Cis-$\Delta^{6,7}$-octadecenic acids (petroselinic acid) is oxidized much more rapidly, its constant K approaching the value of the constant for oleic acid ($\Delta^{9,10}$-octadecenic acid). The oxidation rate of the trans form of petroselinic acid is perceptibly lower than that of the cis form.

SUMMARY

Hydrogenation of petroselinic and petroselaidic acids indicates that petroselinic acid is hydrogenated faster than petroselaidic acid. This circumstance is further proof that petroselinic acid has the cis form. The comparative oxidation with benzoyl hydrogen peroxide of octadecenic acids in which the double bond is located differently in the chain shows that the K constant rises as the double bond's distance from the carboxyl group increases.

The trans form of $\Delta^{6,7}$-octadecenic acid is oxidized more slowly than the cis form.

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[1] In the table, t denotes time, in minutes; v the volume of hydrogen absorbed, mm, reduced to 0° and 760 mm; Δv the number of milliliters of hydrogen absorbed since the previous run; and k the quantity of hydrogen absorbed per minute. Theoretically, 1 g of oleic acid absorbs 79.3 ml of hydrogen.

THE ADDITION OF DIALKYLPHOSPHOROUS ACIDS TO UNSATURATED COMPOUNDS

VI. THE ADDITION OF DIALKYLPHOSPHOROUS ACIDS TO ETHYL CINNAMATE AND ETHYL CROTONATE

A. N. Pudovik

As has been shown in a series of previous papers [1], the addition reaction of dialkylphosphorous acids to electronophilic unsaturated compounds, discovered and developed by us, is a new, quite simple, and convenient method for synthesizing various derivatives and esters of phosphinic acids. The dialkylphosphorous acids, which are typical nucleophilic reagents, are added with great readiness to α, β-unsaturated nitriles, aldehydes, ketones, vinyl esters and esters of carboxylic acids in the presence of alcoholates of the alkali metals.

Except in the case of the unsaturated aldehydes, the reactions follow this pattern:

$$(RO)_2POH + CH_2{=}CH{-}R' \xrightarrow{RONa} (RO)_2\overset{\overset{O}{\|}}{P}{-}CH_2{-}CH_2{-}R'$$

(where R' = CN, COR, OCOR, COOR, and others, and R represents alkyl groups), the dialkylphosphono group being added to the β atom of the double bond. We have used this method to synthesize numerous ketophosphinic esters, cyanophosphinic esters, carboxyphosphinic esters, and some other new types of esters of phosphinic acids [2]. The dialkylphosphorous acids are added to unsaturated aldehydes at the carbonyl group, yielding unsaturated esters of hydroxyphosphinic acids.

Up to the present time only two of the esters of α, β-unsaturated carboxylic acids—methyl acrylate and methyl methacrylate—have been utilized in research into these reactions. It was found that addition to the acrylate takes place much more vigorously, requiring a smaller quantity of the alkali metal alcoholate for its completion than the methacrylate does. In the present paper we report on tests of adding dialkylphosphorous acids to ethyl cinnamate and ethyl crotonate with the objective of further, more detailed and more profound study of this last type of reaction, and, more especially, ascertaining how the nature and the quantity of the substituent groups affects the feasibility and nature of the addition reactions.

The reactions were carried out in the presence of alcoholates of the alkali metals, using the procedure developed by us previously and described in our previous papers.

As might have been expected, the presence of a substituent radical, especially phenyl, at the β carbon atom of the ethylenic bond greatly diminishes its electronophilic character, thus hampering the addition reactions of the dialkylphosphorous acids. These reactions are less vigorous than with methyl acrylate, and require the addition of more alcoholate to the reaction mixture.

We added dimethylphosphorous, diethylphosphorous, diisobutylphosphorous, and dibutylphosphorous acids to the ethyl cinnamate. The constants and yields of the resultant ethyl esters of the β-dialkylphosphono-β-phenylpropionic acids are given in Table 1.

β-Phosphono-β-phenylpropionic acid, with an m.p. of 204°, was secured by saponifying the triethyl ester of β-phosphono-β-phenylpropionic acid.

Similarly, the ethyl esters of β-diethylphosphono- and β-dibutylphosphonobutyric acids were secured by adding diethylphosphorous and dibutylphosphorous acids to ethyl crotonate in the presence of sodium ethoxide. The constants and yields of the resultant products are given in Table 2.

β-Phosphonobutyric acid was secured as a white crystalline powder with an m.p. of 141-143° by saponifying the triethyl ester of β-phosphonobutyric acid.

The mechanism involved in the addition of dialkylphosphorous acids to ethyl cinnamate and ethyl crotonate may be represented as follows:

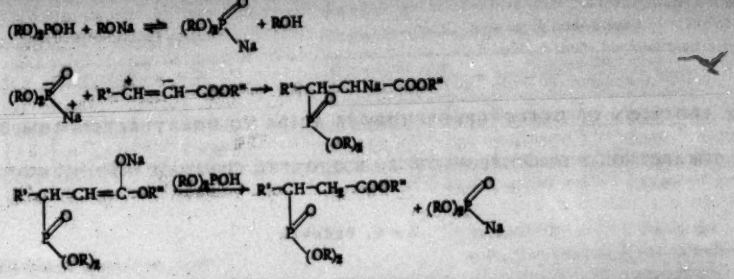

TABLE 1

No.	Formula	Boiling point	n_D^{20}	d_4^{20}	Yield, %
1	$(CH_3O)_2P(O)-CH(C_6H_5)-CH_2-COOC_2H_5$	192° (10 mm)	1.5050	1.1910	85.6
2	$(C_2H_5O)_2P(O)-CH(C_6H_5)-CH_2-COOC_2H_5$	199-200 (11 mm)	1.4917	1.1226	91.1
3	$(iso\text{-}C_3H_7O)_2P(O)-CH(C_6H_5)CH_2COOC_2H_5$	224-225 (14 mm)	1.4800	1.0430	79.0
4	$(n\text{-}C_4H_9O)_2P(O)-CH(C_6H_5)CH_2COOC_2H_5$	231-232 (11 mm)	1.4821	1.0506	81.7

TABLE 2

No.	Formula	Boiling point	n_D^{20}	d_4^{20}	Yield, %
1	$CH_2-CH-CH_2-COOC_2H_5$ $P(O)(OC_2H_5)_2$	146-147° (11 mm)	1.4335	1.0724	77.2
2	$CH_2-CH-CH_2-COOC_2H_5$ $P(O)(OC_2H_5)_2$	186-189 (10 mm)	1.4395	1.0016	58.8

EXPERIMENTAL

Addition of dimethylphosphorous acid to ethyl cinnamate. A saturated solution of sodium ethoxide in absolute methanol was added drop by drop to a mixture of 20.8 g of ethyl cinnamate and 11 g of dimethylphosphorous acid. About 2 ml of solution had to be added to set off the reaction. The latter began abruptly and was accompanied by the evolution of considerable heat by the reaction mixture. After a small amount of additional sodium ethoxide had been added and the reaction mixture had stood for an hour at room temperature, it was distilled from an Arbuzov flask. This yielded 27.2 g of the ethyl ester of β-phenyl-β-dimethylphosphonopropionic acid, with a b.p. of 192° (10 mm); n_D^{20} 1.5050; d_4^{20} 1.1910.

0.1370 g substance: 28.3 ml NaOH (T 0.019589). Found %: P 11.2. $C_{12}H_{17}O_5P$. Calculated %: P 10.9. We also secured a small quantity of low-boiling fractions.

Addition of diethylphosphorous acid to ethyl cinnamate. A solution of sodium ethoxide in absolute ethyl ether was slowly added to a mixture consisting of 15.7 g of ethyl cinnamate and 10.1 g of diethylphosphorous acid. The reaction set in only after considerable ethoxide had been added and was very violent, the ethyl alcohol that had been added to the reaction mixture together with the alcoholate foaming up. Fractionation of the reaction mixture yielded 23.5 g of the triethyl ester of β-phenyl-β-phosphonopropionic acid with a b.p. of 199-200° (11 mm); n_D^{20} 1.4917; d_4^{20} 1.1226.

0.1014 g, 0.1148 g substance: 19.4 ml, 21.3 ml NaOH (T 0.019589). Found %: P 10.3, 10.1. $C_{14}H_{23}O_5P$. Calculated %: P 9.9.

Saponifying the triethyl ester of β-phenyl-β-phosphonopropionic acid. 3.5 grams of the triethyl ester of β-phenyl-β-phosphonopropionic acid was heated in a sealed tube with dilute (1:1) hydrochloric acid. Heating

lasted 6 hours at 130-140°. Repeated evaporation of the solution, to which distilled water was added at intervals, eliminated all of the hydrochloric acid. Crystals settled out of the solution when the latter was carefully evaporated. Recrystallization from water yielded β-phenyl-β-phosphonopropionic acid with an m.p. of 204°.

0.0826 g substance: 20 ml NaOH (T 0.019589). Found %: P 13.1. $C_9H_{11}O_5P$. Calculated %: P 13.4.

Addition of diisobutylphosphorous acid to ethyl cinnamate. The reaction was carried out with 10.4 g of the cinnamate and 9.3 g of diisobutylphosphorous acid in the presence of sodium isobutoxide. The reaction was much quieter than with the lower dialkylphosphorous acids, about 4 ml of a solution of the sodium isobutoxide in isobutyl alcohol having to be added for the reaction to be complete. Fractionation of the reaction mixture yielded 15.5 g of the ethyl ester of β-phenyl-β-diisobutylphosphonopropionic acid, with a b.p. of 224-225° (14 mm); n_D^{20} 1.4800; d_4^{20} 1.0430.

0.1266 g substance: 19.6 ml NaOH (T 0.019589). Found %: P 8.4. $C_{18}H_{31}O_5P$. Calculated %: P 8.4.

Addition of dibutylphosphorous acid to ethyl cinnamate. The same quantities of reagents were used in this reaction as in the previous one, with sodium butoxide present. Fractionation of the reaction mixture yielded 16.1 g of the ethyl ester of β-phenyl-β-dibutylphosphonopropionic acid, with a b.p. of 231-232° (11 mm); n_D^{20} 1.4821; d_4^{20} 1.0506.

0.1200 g, 0.1374 g substance: 18.2 ml, 20.5 ml NaOH (T 0.019589). Found %: P 8.2, 8.1. $C_{18}H_{31}O_5P$. Calculated %: P 8.4.

Addition of diethylphosphorous acid to ethyl crotonate. A solution of sodium ethoxide in absolute ethyl alcohol was added drop by drop to a mixture consisting of 9 g of ethyl crotonate and 11.2 g of diethylphosphorous acid. The reaction was more energetic, and less of the ethoxide was required than was the case in the analogous reaction with ethyl cinnamate. Fractionation of the reaction mixture yielded 15.6 g of the triethyl ester of β-phosphonobutyric acid, with a b.p. of 146-147° (11 mm); n_D^{20} 1.4335; d_4^{20} 1.0724.

0.1496 g, 0.1306 g substance: 38.2 ml, 33.6 ml NaOH (T 0.01768). Found %: P 12.5, 12.6. $C_{10}H_{21}O_5P$. Calculated %: P 12.3.

Saponifying the triethyl ester of β-phosphonobutyric acid. 5 grams of the triethyl ester of β-phosphonobutyric acid was heated to 150° in a sealed tube for 5 hours with 30 ml of dilute (1:1) hydrochloric acid. After the tube was opened, the layer of ethyl chloride that had separated out was removed, and the aqueous solution was repeatedly evaporated distilled water being added at intervals, until all the hydrochloric acid had been eliminated. Crystals of β-phosphonobutyric acid settled out of the solution when it had been evaporated to 15-20 ml. They had an m.p. of 141-143° after recrystallization from water.

0.1390 g substance: 52.5 ml NaOH (T 0.017688). 0.1088 g substance: 41 ml NaOH (T 0.01784). Found %: P 18.5, 18.6. $C_4H_9O_5P$. Calculated %: P 18.5.

Addition of dibutylphosphorous acid to ethyl crotonate. Sodium butoxide dissolved in butyl alcohol was added to a mixture consisting of 7.2 g of the crotonate and 12 g of dibutylphosphorous acid. Fractionation of the reaction mixture yielded 11.3 g of the ethyl ester of β-dibutylphosphonobutyric acid, with a b.p. of 186-189° (10 mm); n_D^{20} 1.4395; d_4^{20} 1.0016.

0.1794 g, 0.1268 g substance: 35.4 ml, 25.4 ml NaOH (T 0.01768). Found %: P 9.7, 9.8. $C_{16}H_{33}O_5P$. Calculated %: P 10.06.

SUMMARY

It has been shown that in the presence of alcoholates of the alkali metals dialkylphosphorous acids are readily added to ethyl cinnamate and ethyl crotonate, yielding the ethyl ester of β-dialkylphosphono-β-phenylpropionic and β-dialkylphosphonobutyric acids, respectively. Saponification of the latter yielded β-phosphono-β-phenylpropionic and β-phosphonobutyric acids.

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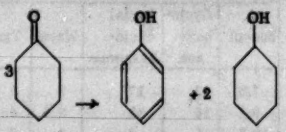
THE CATALYTIC CONVERSION OF CYCLOHEXANONE AND 1,3-DIMETHYLCYCLOPENTAN-5-ONE OVER ALUMINA

I. N. Nazarov, I. L. Kotlyarevsky, and N. V. Kuznetsov

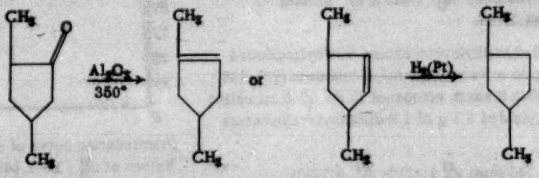
The discovery of irreversible catalysis in 1911 by Zelinsky [1] was followed by a multiplicity of papers devoted to a study of this phenomenon in the most diversified organic compounds [2]. Terentyev and Guseva [3] were the first to make a thorough study of the catalytic conversions of cyclohexanone, showing that cyclohexanone is converted into cyclohexanol and phenol, with a good yield, at temperatures of the order of 230-250° over a palladium catalyst:



In the great majority of cases the phenomenon of irreversible catalysis has been observed with hydrogenation-dehydrogenation catalysts. The sole instances of irreversible catalysis over alumina are the conversion of cyclohexene into benzene observed by Petrov [4], the yield being negligible, and the formation of phenol when cyclohexanol is passed over alumina, observed by Bartlett and Woods [5].

In the course of our investigation of cyclic ketones, we decided to look into the behavior of cyclohexanone and 1,3-dimethylcyclopentan-5-one over alumina. We found that cyclohexanone undergoes the same transformations over alumina (into phenol and cyclohexanol) in the temperature range from 390 to 450° that had been previously observed to occur over Pd, the cyclohexanol being completely dehydrated into cyclohexene under the conditions of the experiment.

About 30% of 1,3-dimethylcyclopentan-5-one is converted into 1,3-dimethylcyclopentene over alumina at 350°, the product absorbing 1 mole of hydrogen when hydrogenated with a Pt catalyst and yielding the 1,3-dimethylcyclopentane described previously [6]:



In this process a slight amount of 1,3-dimethylcyclopentadiene is also produced apparently.

EXPERIMENTAL

Catalytic conversion of cyclohexanone. Cyclohexanone (b.p. 155°; n_D^{20} 1.4506), was passed at a fixed rate of flow through a catalytic tube 22 mm in diameter, made of molybdenum glass and filled for 80 cm of its length with granulated alumina 2-3 mm in diameter. The resultant catalyzate separated into two layers—aqueous and organic. Cyclohexene was distilled from the organic layer up to 90°. An ether extract of the aqueous layer was combined with the aqueous layer, the ether was driven off, and a 90-200° fraction was distilled. The tarry residue was weighed. The 90-200° fraction was processed with a 10% alkali solution to remove the phenol, the

alkaline solution of the phenolate being treated with ether. The ether extract was combined with the neutral residue of the 90-200° fraction. The product was dried with magnesium sulfate and distilled, the cyclohexanone recovered after the experiment being collected in the 152-156° range. The phenolate solution was acidulated with dilute (1:1) hydrochloric acid, and the phenol was thoroughly extracted with ether. The ether extract was dried with magnesium sulfate, the ether was driven off, and the phenol was distilled at 179-183°, crystallizing into its characteristic crystals upon cooling. The phenol was used to prepare tribromophenol with an m.p. of 92-93° and triiodophenol with an m.p. of 157°. The mixed melting points with synthetic samples exhibited no depression. The crude cyclohexene was dried with fused calcium chloride and was collected in the 78-83° range upon distillation. All the cyclohexanone fractions collected in the several runs were combined and fractionated with a column having the efficiency of 14 theoretical plates. We fractionated 75 g of the cyclohexene, which yielded:

Fraction 1, b.p. 77-82.5, 8 g; Fraction 2, 82.5-82.9 def, 59 g; n_D^{20} 1.4451; d_4^{20} 0.8104; residue 5 g; fractionation losses 3 g.

The cyclohexene was used to produce dibromocyclohexane, with a b.p. of 100-101° at 14 mm.

Our data on the conversion of cyclohexanone over alumina under various conditions are given in the following table.

Run	Temperature, °	Rate of flow of cyclohexanone, ml/hr	Amount of cyclohexanone passed through, g	Grams secured					% conversion
				Phenol	Cyclohexene	Initial cyclohexanone	Water	Tar	
1	390°	200	50	7.8	13	17	3	5	50
2	400	150	50	9.1	16	12	3.5	6	60
3	400	100	50	10.8	19	6	4	6	70
4	420	100	50	11.6	20.5	–	4.5	9	75
5	450	100	50	9.3	16.5	–	4	16	60

Catalytic conversion of 1,3-dimethylcyclopentan-5-one over alumina. 1,3-Dimethylcyclopentan-5-one (b.p. 149.5-150° at 750 mm; n_D^{20} 1.4325) [7], prepared by hydrogenating 1,3-dimethyl-$\Delta^{4,5}$-cyclopenten-5-one with a Raney Ni catalyst and fractionation into a column with an efficiency of 14 theoretical plates, was passed through the catalytic tube described in the preceding experiment. 94 grams of 1,3-dimethylcyclopentan-5-one was passed over alumina at 350° and at a rate of 20 g/hr. This yielded 66 g of catalyzate, from which 10 g of water was eliminated. The organic layer of the catalyzate was dried with magnesium sulfate and fractionated, yielding two fractions:

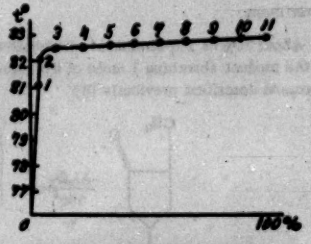
Fraction 1, b.p. 84-96°, 31 g; and Fraction 2, b.p. 35-140° at 20 mm, 16 g.

Fractionating Fraction 1 into a column with an efficiency of 22 theoretical plates yielded 15 g of 1,3-dimethylcyclopentene:

B.p. 92-92.3° at 750 mm; n_D^{20} 1.4337; d_4^{20} 0.7748; MR 32.35; calculated 31.84.

6.85 g of the 1,3-dimethylcyclopentene was hydrogenated with a Pt catalyst, using no solvent, 1800 ml of hydrogen (20°, 748 mm) being absorbed within 2 hours, compared to the 1740 ml called for by theory. Fraction yielded 6.5 g of 1,3-dimethylcyclopentane [6].

B.p. 90-90.1° at 746 mm; n_D^{20} 1.4117; d_4^{20} 0.7457; MR 32.75; calculated 32.31.



Fractionation curve of cyclohexene. Values of n_D^{20}: 1 - 1.4492; 2 - 1.4467; 3 - 1.4455; 4 - 1.4453; 5 - 1.4450; 6 - 1.4452; 7 - 1.4450; 8 - 1.4450; 9 - 1.4450; 10 - 1.4450; 11 - 1.4450.

SUMMARY

Cyclohexanone is converted into phenol and cyclohexene over alumina at 390-450°, the yield being high (up to 75%). Under similar conditions 1,3-dimethylcyclopentan-5-one is converted into 1,3-dimethylcyclopentene, the yield being 30%, plus a small amount of 1,3-dimethylcyclopentadiene.

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RESEARCH ON THE CYCLIC ACETALS OF HYDROXY CARBONYL COMPOUNDS

III. TRANSFORMATION OF THE METHYL LACTOLIDE OF METHYLBENZOYLCARBINOL WHEN ACTED UPON BY ACID AND ALKALINE REAGENTS[1]

T. I. Temnikova and E. N. Kropacheva

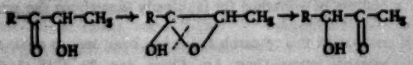
The method of synthesizing the methyl lactolides of α ketols [1] developed by us in the synthesis of α-methoxy-α-phenylpropylene oxide (I) makes it possible to make a comprehensive study of these α ketol derivatives, which are highly interesting theoretically, though they are altogether unexplored.

Investigation into the behavior of the methyl lactolides of the α ketols when they are reacted with acid and alkaline reagents is of interest in shedding light on the influence of the methoxy group upon the sequence in which the oxide ring is ruptured during addition reactions and in isomeric transformations, and in confirming the correctness of our concepts of the origin of similarly structured α alcohol oxide groups as intermediate products in the isomeric transformations of α ketols in an acid medium.

Theoretical consideration [2] might lead us to suppose that the oxide ring of (I) will be ruptured in an acid medium at the phenyl nucleus and methoxy group end, inasmuch as the C-O bond ought to be more highly polarized at these groups in oxonium compounds in an acid medium owing to the presence of electromeric effects in these groups.

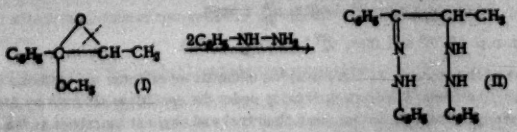
It is impossible to predict the sequence in which an oxide ring will be ruptured when a methoxy ether reacts with nucleophilic reagents, since the point at which reaction takes place with the reagent in reactions of this type is governed not only by the polarizability of the bonds and the distribution of the positive charges on the carbon atoms of the methoxy ether, but also by the steric accessibility of the reaction center.

In connection with the hypotheses advanced by A. E. Favorsky previously on the formation of α-alcohols-oxidic ring compounds as intermediate products during the isomeric transformations of α-ketols in an acid medium [4]:



we were interested in finding the conditions required for converting the methyl lactolide of methylbenzoylcarbinol into a methyl ester of a ketol i.e., in performing an isomeric transformation without changing the composition of the molecule.

These questions were settled only partially in our previous papers [1, 3], it having been shown that the action of phenylhydrazine gives rise to phenylhydrazidophenylhydrazone (II), the formation of which can be explained only on the assumption that the methoxy ether (I) is initially ruptured at the methyl group end:



[1] Note added in proof. Brief communication printed in the Proc. U.S.S.R. Acad. Sci. 78, 291 (1951).

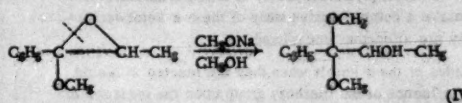
When the ether is reacted with a 10% aqueous solution of potash, it is hydrolyzed, an α ketol being produced [3]. The problem of the order in which the oxide ring is ruptured during hydrolysis is unsolved.

In the present paper we made a study of the following reactions: the action of methanol and of sodium methoxide in ether and in a methanol solution upon the methyl lactolide of methylbenzoylcarbinol and the transformations of the methyl lactolide when reacted with acids.

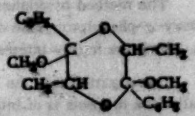
As has been pointed out earlier, the methyl lactolide of methylbenzoylcarbinol reacts violently with ethyl alcohol [1]. The reaction is also accompanied by foaming when it is poured into methanol, the principal reaction product being the cyclodimethyl dilactolide of methylbenzoylcarbinol (III) as acicular white crystals with an m.p. of 244-245°. As has been pointed out previously [5] this same dilactolide is secured when methylbenzoylcarbinol is reacted with 3% HCl in methanol. The mixed melting point of the two preparations exhibited no depression. A slight quantity of acetylbenzoyl was recovered in addition to the dimer.

In this connection, it is worthy of note that when a 3% HCl reacted with the same methyl lactolide (I) in methanol we secured the cyclodimethyl dilactolide of the isomeric ketol-phenylacetylcarbinol [1].

When the methyl lactolide of methylbenzoylcarbinol (I) was reacted with sodium methoxide in methanol we secured the dimethyl ketal of methylbenzoylcarbinol (IV):



(IV)



(III)

The substance is a liquid with a b.p. of 76-76.5° at 2 mm[1]. The dimethyl ketal of the isomeric ketol-phenylacetylcarbinol – is a crystalline substance with an m.p. of 62-63° according to McPhee and Klingsberg [6]. Hydrolysis of the dimethyl ketal we had synthesized yields methylbenzoylcarbinol. The dimethyl ketal of methylbenzoylcarbinol proved to be an unstable substance, slowly turning into the cyclodimethyl dilactolide of methylbenzoylcarbinol, with an m.p. of 244-245° (III), when stored. Other authors [7] have also observed that dimethyl ketals are converted into cyclodimethyl dilactolides.

It has thus been proved that the oxide ring of a methyl lactolide is ruptured by the action of sodium methoxide at the phenyl ring and methoxy group end, i.e., the CH_3O^- moves during the reaction to the carbon atom that possesses a bigger positive charge and a greater ability to coordinate with the negatively charged group, because of the presence of a phenyl ring attached to that same carbon atom.

Some tarring occurs when the methyl lactolide (I) is heated with anhydrous sodium methoxide in an ether solution or when it is distilled over sodium methoxide, though the methyl lactolide is recovered unchanged.

Investigation of the products obtained as the result of the action of acid reagents upon the methyl lactolide of methylbenzoylcarbinol required the development of a method for faultlessly identifying the reaction products.

[1] Note added during proofs. After we had completed this research and it had been sent to press a paper by Stevens, Malik and Pratt appeared in an American chemical journal (Jour. Am. Chem. Soc. 72, 4758 (1950) in which they describe some transformations of the methyl lactolide of methylbenzoylcarbinol we had synthesized earlier [1], especially its reaction with methanol in the presence of CH_3ONa. The American authors describe the substance they isolated in this reaction as a dimethyl ketal, whose boiling point differs from that of our preparation (94-95° at 0.5 mm). It should also be noted that the methyl lactolide that Stevens, Malik, and Pratt synthesized from α-chloroethyl phenyl ketone, which had the same chemical properties and in part the same physical properties as our preparation synthesized from α-bromoethyl phenyl ketone, had a very much different boiling point.

Our preparation: b.p. 64-65° at 4 mm; d_4^{20} 1.0618; n_D^{20} 1.5080.

Stevens' preparation: b.p. 75-76° at 1 mm; d_4^{25} 1.052; n_D^{25} 1.5002.

After the publication of the research by the American chemists we effected the synthesis of the methyl lactolide from α-chloroethyl phenyl ketone and sodium methoxide under the conditions set forth by Stevens and his associates: the substance we secured had exactly the same chemical and physical properties as the methyl lactolide we had previously synthesized from α-bromoethyl phenyl ketone.

enabling us to determine isomeric compounds when they are present together. What was particularly necessary was the development of a method for establishing the structure of the methyl ethers of α ketols and identifying them. The methyl ether of phenylacetylcarbinol has been synthesized by Auwers [8], its constants being as follows:

b.p. 78-79° at 1 mm; n_D^{20} 1.5220; semicarbazone m.p. 157-158°.

We synthesized the methyl ether of methylbenzoylcarbinol, which is not described in the literature,[1]) by methylating methylbenzoylcarbinol with methyl iodide in the presence of silver oxide; its constants were as follows:

b.p. 79-80° at 1 mm; d_4^{20} 1.071; n_D^{20} 1.5225; semicarbazone m.p. 159-160°.

The foregoing comparison indicates that the two isomeric ethers have practically the same constants; we found that the mixed melting point of the semicarbazones exhibited only very slight depression. Nor were we able to identify the methyl ethers of α ketols by the method ordinarily employed to identify the ketols themselves — converting them into glycols by means of organomagnesium compounds and then oxidizing them [4,9] — inasmuch as the glycol ethers can be oxidized only under extremely severe conditions.

We therefore decided to utilize the spectroscopic method of identifying substances by the absorption curves in the ultraviolet. Comparison of the absorption curves of the various isomeric substances containing a carbonyl group [10] and of the absorption curves of the compounds we had recorded (Fig. 1) showed that whenever a compound contained a benzoyl ring there was a slight maximum on the absorption curve in the 320-330 mμ wavelength region.

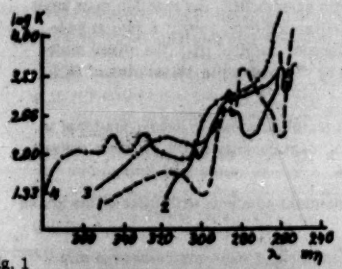


Fig. 1
1 - Ethyl phenyl ketone; 2 - methyl benzyl ketone; 3 - benzoin; 4 - methyl ether of benzoin.

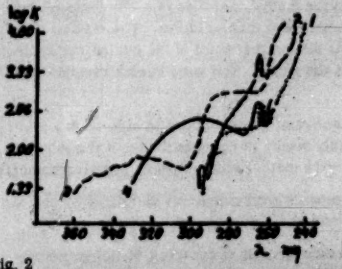


Fig. 2
1 - methyl lactolide of methylbenzoylcarbinol; 2) dimethyl ketal of methylbenzoylcarbinol; 3 - methyl ether of methylbenzoylcarbinol; 4 - methyl ether of phenylacetylcarbinol.

The methyl ethers of the ketols, which have nearly identical physical properties, can be identified by their ultraviolet absorption spectra because of the presence of a benzoyl ring in the methyl ether of methylbenzoylcarbinol and the absence of such a ring in phenylacetylcarbinol. (Fig. 2).[2]) In this same graph we have plotted the absorption curve of the methyl lactolide of methylbenzoylcarbinol (I) and the dimethyl ketal of methylbenzoylcarbinol. The absorption curves of the two compounds look alike, which indicates the similarity in their structures — the two compounds are ketals of the same ketol. The methyl lactolide of methylbenzoylcarbinol differs from its isomeric methyl ethers of methylbenzoylcarbinol and of phenylacetylcarbinol in not having an absorption maximum in the absorption region of the carbonyl group.

We managed to effect the isomeric conversion of the methyl lactolide only by the action of strong mineral acids in a benzene solution.

When an aqueous solution of the methyl lactolide is reacted with a 1% aqueous solution of hydrochloric or

[1]) Note added during proofs: In the paper by Stevens, Malik and Pratt (cf p. 1198) the methyl ether of methylbenzoylcarbinol was produced by reacting C_6H_5MgBr with $CH_3CH(OCH_3)CH$, its b.p. being 76-77° at 0.8 mm; d_4^{20} 1.095; n_D^{20} 1.5220; semicarbazone m.p. 161-162°.

[2]) The photographs were made with the SP-22 spectrograph, using a variable-width cell and the Henri method [11]. Absolute diethyl ether was employed as the solvent.

oxalic acid, the oxide ring is hydrolyzed and methylbenzoylcarbinol $C_6H_5CO-CHOH-CH_3$ is produced, as was proved by comparing the physical constants, conversion into a glycol: 1,2-diphenylpropanediol-1,2 with an m.p. of 91-92°, and comparing the absorption spectra in the ultraviolet (Fig. 3).

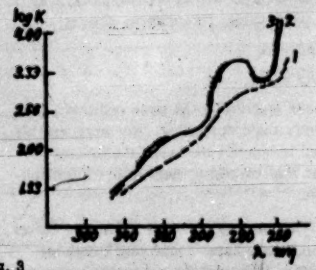


Fig. 3
1 - Phenylacetylcarbinol; 2 - methylbenzoylcarbinol; 3 - product of the reaction of the methyl lactolide of methylbenzoylcarbinol with aqueous solutions of acids.

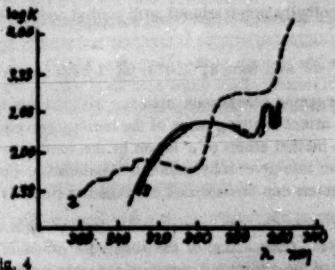


Fig. 4
1 - Methyl ether of phenylacetylcarbinol; 2 - methyl-ether of methylbenzoylcarbinol; 3 - product of the isomerization of the methyl lactolide of methylbenzoyl-carbinol.

When the methyl lactolide of methylbenzoylcarbinol is reacted with gaseous HCl, the reaction mass heats up greatly, foams, and then solidifies. The crystals obtained after recrystallization from methanol fuse at 244-246°, which is the melting point of the cyclodimethyl lactolide of methylbenzoylcarbinol (III) (the mixed melting point was the same). The same cyclodimethyldilactolide is produced by the action of a 1% solution of HCl in benzene.

The action of anhydrous oxalic acid upon a solution of the methyl lactolide of methylbenzoylcarbinol in benzene mainly results in polymerization of the substance, only an insignificant quantity of the isomeric conversion product — the methyl ether of phenylacetylcarbinol (IV) being secured.

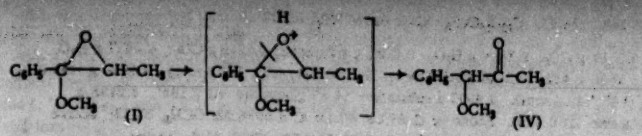
The product synthesized was identified by comparing its physicochemical constants with those of the known synthesized methyl ether of phenylacetylcarbinol [8].

Substance secured as the result of isomerization: b.p. 79-80° at 1 mm; n_D^{20} 1.520; semicarbazone m.p. 156-157°.

Methyl ether of phenylacetylcarbinol: b.p. 78-79° at 1 mm; n_D^{20} 1.522; semicarbazone m.p. 157-158°.

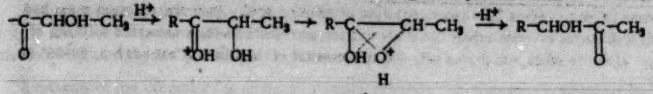
The mixed melting point of the semicarbazone prepared from the isomerization product and the known preparation of the semicarbazone of the methyl ether of phenylacetylcarbinol exhibited no depression. The methyl ether was also identified as an individual substance by comparing the absorption curves (in the ultraviolet) of the isomeric ethers with those of the product synthesized as the result of isomeric conversion (Fig. 4). The shape of the absorption curve of the isomerization product is evidence of the individuality of the synthesized ether. If the isomerization of the methoxy ether were to take place in part as the result of rupture of the oxide ring at the methyl group, yielding the methyl ether of methylbenzoylcarbinol (a less likely reaction product), the presence of the latter in the mixture could be detected by the appearance of even a slight maximum in the 320-330 mμ wavelength region, which was not found to be the case. As might have been expected, the isomeric conversion took place entirely in one direction: the oxide ring was ruptured at the carbon atom that was connected to the phenyl and methoxy groups. The same sort of isomerization was found when the methyl lactolide (I) was reacted in benzene with dichloroacetic acid.

We thus were able in the present research to effect the isomeric conversion of the methyl lactolide of methylbenzoylcarbinol into an ether of phenylacetylcarbinol, in this way experimentally corroborating the second stage of the schema suggested by A. E. Favorsky for the mechanism involved in the isomeric conversion of α-lactols in an acid medium.



(I) (IV)

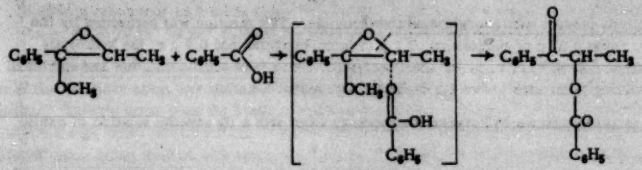
Bearing in mind the part played by the acid's proton in the isomerization of α-ketols and the high probability that an oxonium compound is formed by the oxygen of the carbonyl group, we can represent A. E. Favorsky's schema for the isomeric transformation of the α-ketols in the following more precise form:



When a dilute benzene solution of benzoic acid acts upon the methyl lactolide of methylbenzoylcarbinol, the sole reaction product is the bonzoic ether of methylbenzoylcarbinol as a compound with an m.p. of 180° that is very slightly soluble in ether.

The mixed melting point of the compound with the ether prepared from α-bromoethyl phenyl ketone and potassium benzoate exhibited no depression. The structure of the benzoic ether had been previously established in a paper by A. E Favorsky and T I. Temnikova [9]. As was proved in that same paper, the benzoic ether of phenylacetylcarbinol has totally different properties – it is freely soluble in ether and its m.p. is 51.4-52.5°.

Hence, whereas benzene solutions of oxalic and dichloroacetic acids react with the methyl lactolide of methylbenzoylcarbinol as the result of the catalytic action of the hydrogen ions as isomerizing agents, a weak organic acid, such as benzoic acid, reacts with the methyl lactolide as a weak base, the oxide ring being ruptured at the methyl group, as in the reaction with phenylhydrazine:



When we compare these two observations: the rupture of the oxide ring at the methyl group when benzoic acid reacts with phenylhydrazine and the rupture of the oxide ring at the other end (the phenyl and methoxy groups) when it reacts with sodium methoxide, we see that nucleophilic reagents can enter into reaction with the primary ring attacked in various ways. It may be that a steric factor plays a decisive part in the case of phenylhydrazine or benzoic acid.

EXPERIMENTAL

Reaction of the methyl lactolide of methylbenzoylcarbinol with methanol. Six grams of the methoxy ether was added a drop at a time, with constant stirring, to 25 ml of absolute methanol, causing the reaction mixture to foam. Driving off the alcohol yielded a crystalline substance and a dark-yellow liquid. The melting point of the crystals was 244-245° after recrystallization from methanol. Yield: 4 g. Their mixed melting point with the known cyclodimethyl dilactolide of methylbenzoylcarbinol exhibited no depression.

The yellow oil was distilled in vacuo: b.p. 78-82° at 2 mm; n_D^{20} 1.533; 0.58 g yield.

The semicarbazone prepared from this liquid had an m.p. of 226-228° and exhibited no depression of the melting point when mixed with the known disemicarbazone of acetylbenzoyl (m.p. 227-228°).

Reaction of the methyl lactolide of methylbenzoylcarbinol with sodium methoxide in methanol. Seven grams of the methoxy ether was added to a solution of sodium methoxide, prepared from 5 g of sodium in 100 ml of methanol. The mixture was heated for three hours on a water bath. Then a current of carbon dioxide was passed through the solution for 12 hours until no more soda was thrown down. The solution was separated from the precipitate. The methanol was driven off in vacuo, the residual liquid being washed with water and extracted with ether. The ether extract was dried with $MgSO_4$. The ether was driven off, and the residual oil fractionated in vacuo: the bulk of the oil distilled at 76-76,5° at 2 mm; 3.12 g yield.

d_4^{20} 1090; n_D^{20} 1.5127; MR_D 54.08. $C_{11}H_{16}O_3F_3$. Calculated MR_D 54.32.

0.1446 g substance: 0.3508 g CO_2; 0.1034 g H_2O. 0.0921 g substance: 0.2269 g CO_2; 0.0677 g H_2O. 0.1501 g substance: 0.3550 g AgI. 0.1128 g substance: 13.2 ml CH_4 (12°, 749.9 mm). 0.1020 g substance: 11.3 ml CH_4 (14°, 749.4 mm). 0.0996 g substance; 14.57 g benzene Δt 0.185°. 0.2158 g substance; 14.57 g benzene Δt 0.400°. Found %: C 67.55, 67.19; C 8.00, 8.22; OCH_3 31.22; active H 0.97, 0.92; M 189, 190. $C_{11}H_{16}O_3$. Calculated %: C 67.32; H 8.21; OCH_3 31.6; active H 1; M 196.

Hydrolysis of the dimethyl ketal of methylbenzoylcarbinol. Two grams of the dimethyl ketal was heated on a water bath, with constant stirring, with a 5% aqueous solution of sulfuric acid. After the reaction mass had cooled the reaction product was extracted with ether; the ether extract was washed with a saturated solution of soda and dried over $MgSO_4$. Then the ether was driven off, and the residual oil distilled in vacuo: b.p. 84-86° at 2 mm; n_D^{20} 1.543.

The substance secured after hydrolysis (0.5 g) was added to benzenemagnesium bromide, prepared from 0.45 g of magnesium and 3.15 g of bromobenzene. The reaction product's m.p. was 91-92° after recrystallization from petroleum ether. Its mixed melting point with known 1,1-diphenylpropanediol-1,2 exhibited no depression.

Conversion of the dimethyl ketal of methylbenzoylcarbinol into the cyclodimethyl dilactolide of methylbenzoylcarbinol. Within a week after its synthesis the dimethyl ketal turned into a crystalline mass. Its melting point was 244-245° after recrystallization from methanol. Its mixed melting point with a known sample of the cyclodimethyl dilactolide of methylbenzoylcarbinol exhibited no depression.

Reaction of the methyl lactolide of methylbenzoylcarbinol with a 1% aqueous solution of HCl or oxalic acid. One gram of the methoxy ether was added, with chilling and stirring, to a 1% aqueous solution of hydrogen chloride. The next day the product was extracted with ether, the ether extract dried with $MgSO_4$, the ether driven off, and the oily residue fractionated in vacuo: b.p. 86-88° at 2 mm; n_D^{20} 1.543. [1])

Reaction of the hydrolysis product with phenylmagnesium bromide. This reaction was performed by the method described previously, using 0.33 g of magnesium 2.1 g of bromobenzene, and 0.5 g of the hydrolysis product. The resultant substance had an m.p. of 91-92° after recrystallization from petroleum ether and exhibited no depression of its mixed melting point with known 1,1-diphenylpropanediol-1,2.

Similar results were secured when we hydrolyzed the methoxy ether with a 1% aqueous solution of oxalic acid.

Reaction of the methyl lactolide of methylbenzoylcarbinol with gaseous hydrogen chloride. A current of anhydrous gaseous hydrogen chloride was passed through a flask containing 0.6 g of the methoxy ether; the reaction mass warmed up considerably and then foamed. The entire mass crystallized upon cooling. The crystals were washed with ether and recrystallized from methanol; m.p. 244-245° Their mixed melting point with the known cyclodimethyl dilactolide of methylbenzoylcarbinol (whose m.p. was 244-245°) exhibited no depression.

Reaction of the methyl lactolide of methylbenzoylcarbinol with a 1% solution of HCl in benzene. A solution of 8 g of the methoxy ether in benzene was added a drop at a time, with stirring and chilling, to a 1% solution of hydrogen chloride in benzene. The reaction was accompanied by the evolution of heat. Twelve hours later the hydrogen chloride and the benzene were driven off in vacuo with gentle heat, leaving behind a mixture of crystals with a brown oil. The crystals were filtered out of the oil, washed with ether, and recrystallized from methanol; their m.p. was 245°; 3.4 g yield. Their mixed melting point with the known cyclodimethyl dilactolide of methylbenzoylcarbinol exhibited no depression.

The oil left after the crystals had been filtered out was treated with an aqueous soda solution and then extracted with ether. The ether extract was dried over $MgSO_4$, the ether driven off, and the oily residue distilled in vacuo: Fraction I 76-84° at 3 mm – 0.25 g; n_D^{20} 1.529; Fraction II 85-87° at 3 mm – 0.56 g; n_D^{20} 1.525; Fraction III, 87-91° at 3 mm – 1.14 g; n_D^{20} 1.525.

All three fractions contained a halogen (determined by a Beilstein test); they were not analyzed further.

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[1]) The figures given in the literature for methylbenzoylcarbinol are: b.p. 123° at 14 mm; n_D^{20} 1.5420 [8].

Reaction of the methyl lactolide of methylbenzoylcarbinol with oxalic acid in benzene. Nine grams of the methoxy ether was added drop by drop with constant stirring to 0.5 g of the oxalic acid suspended in 130 ml of benzene. The oxalic acid gradually dissolved. The next day the benzene solution was washed with a saturated soda solution and then dried over $MgSO_4$. The benzene was driven off, and the remaining oil fractionated in vacuo: Fraction I, 76-79° at 1 mm – 2.11 g; n_D^{20} 1.520; Fraction II, 80-110° at 1 mm – 0.56 g; n_D^{20} 1.528; Fraction III, 240-242° at 1 mm – 4.2 g.

Molecular weight of Fraction III: 0.1131 g substance; 17.8 g benzene; Δt 0.097°. 0.2610 g substance; 17.8 g benzene; Δt 0.235°. Found M: 336.4, 320. $C_{20}H_{24}O_4$. Calculated M: 328.

When Fraction I was mixed with a water-alcohol solution of semicarbazide, we secured white crystals with an m.p. of 156-157°. Their mixed melting point with the known semicarbazone of the methyl ether of phenylacetylcarbinol (m.p. 157-158°) exhibited no depression.

Synthesis of the methyl ether of methylbenzoylcarbinol. Five grams of methylbenzoylcarbinol was heated for 10 hours, with constant stirring, in absolute ether with 15.7 g of silver oxide and 32 g of methyl iodide. When the reaction was over, the ether solution was filtered free of the precipitate, the ether and the methyl iodide driven off, and the remaining oil fractionated in vacuo: b.p. 79-80° at 1 mm. This yielded 4.5 g (82% of the theoretical) of a highly mobile, light-yellow liquid.

d_4^{20} 1.0704; n_D^{20} 1.5225; MR_D 46.77. $C_{10}H_{12}O_2$. Calculated MR_D 46.43.

0.0893 g substance: 0.2402 g CO_2; 0.0574 g H_2O. 0.0920 g substance: 0.2461 g CO_2; 0.0613 g H_2O. 0.0991 g substance: 0.1433 g AgI. Found %: C 73.41, 79.00; H 7.19, 7.46; OCH_3 19.09. $C_{10}H_{12}O_2$. Calculated %: C 73.17; H 7.31; OCH_3 18.9.

When the solution was mixed with semicarbazide, we obtained the semicarbazone, which had an m.p. of 159-160° after recrystallization from alcohol.

0.0854 g substance: 14.2 ml N_2 (20°, 760.6 mm). 0.0878 g substance: 14.7 ml N_2 (20°, 760.6 mm). Found %: N 19.12, 19.23. $C_{11}H_{15}O_2N_3$. Calculated %: N 19.0.

Reaction of the methyl lactolide of methylbenzoylcarbinol with a benzene solution of benzoic acid. Two grams of the methoxy ether was added drop by drop, with chilling, to a solution of 2 g of benzoic acid in 50 ml of benzene. Twelve hours later the benzene solution was washed with a solution of soda and dried over $MgSO_4$, after which the benzene was driven off. The oil left behind solidified at once. The resulting crystals had an m.p. of 107-108° after being washed with ether. Yield 2 g. Their mixed melting point with the known benzoic ether of methylbenzoylcarbinol (m.p. 108°) exhibited no depression.

Reaction of the methyl lactolide of methylbenzoylcarbinol with a benzene solution of dichloroacetic acid. Nine grams of the methoxy ether was added drop by drop, with constant stirring to 0.6 g of dichloroacetic acid in 150 ml of benzene. The next day the reaction mixture was washed with a saturated soda solution and dried over $MgSO_4$. The benzene was driven off, and the remaining oil was fractionated in vacuum: Fraction I, 85-87° at 4-5 mm – 0.82 g; n_D^{20} 1.520. Fraction II, 87-88° at 4-5 mm – 2.72 g; n_D^{20} 1.521. Fraction III, 260-262° at 4-5 mm – 3.8 g.

Fractions I and II yielded a semicarbazone with an m.p. of 156-157° when treated with a water-alcohol solution of semicarbazide acetate. Its mixed melting point with the known semicarbazone of the methyl ether of phenylacetylcarbinol exhibited no depression.

Molecular weight of Fraction III. 0.1144 g substance; 18.2 g benzene; Δt 0.102°. 0.2959 g substance; 18.2 g benzene; Δt 0.242°. Found M: 316.1, 338.0. $C_{20}H_{24}O_4$. Calculated M: 328.

SUMMARY

1. It has been shown that the dimethyl ketal of methylbenzoylcarbinol is produced by the reaction of the methyllactolide of methylbenzoylcarbinol with sodium methoxide dissolved in methanol. When the methyl lactolide is reacted with anhydrous sodium methoxide in ether or at high temperature without a solvent, the methyl lactolide is recovered unchanged.

2. The action of pure methanol or anhydrous HCl, either in the gaseous state or dissolved in benzene, upon

the methyl lactolide of methylbenzoylcarbinol results in dimerization, the product being the cyclodimethyl dilactolide of methylbenzoylcarbinol.

3. Aqueous solutions of HCl or of oxalic acid acting upon a methyl lactolide hydrolyze the oxide ring, producing methylbenzoylcarbinol.

4. The action of benzene solutions of oxalic or dichloroacetic acid upon the methyl lactolide of methylbenzoylcarbinol isomerizes it, producing the methyl ether of phenylacetylcarbinol.

5. The action of a benzene solution of benzoic acid upon the methyl lactolide of methylbenzoylcarbinol produces the benzoic ether of methylbenzoylcarbinol.

6. Methylbenzoylcarbinol, phenylacetylcarbinol, and their derivatives were identified by their absorption spectra in the ultraviolet.

In conclusion, we wish to express our gratitude to S. N. Andreev for his aid and advice in the spectroscopic analysis.

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* See Consultants Bureau translation, p. a-983.

** See Consultants Bureau translation, p. a-541.

*** See Consultants Bureau translation, p. 199.

THE REACTION OF ALDEHYDES AND KETONES WITH ACETIC ANHYDRIDE

I. SYNTHESIS OF CYCLOHEXENYL-Δ_1-ACETATE AND CYCLOHEXYLIDENE DIACETATE FROM CYCLOHEXANONE

I. V. Machinskaya

Although it is very easy to prepare diacyl derivatives of the hydrated form of aldehydes, some of them, such as ethylidene diacetate, being employed in industry, no diacyl derivatives of the hydrated form of ketones have been synthesized as yet [1]. Analogous diacetyl derivatives of the aldehydes are readily synthesized by reacting acetic anhydride with aldehydes in the presence of minute quantities of concentrated sulfuric acid [2]. The ketones either do not react with acetic anhydride at all [3], or else the action of acetic anhydride in the presence of various catalysts yields either enolic forms of the acetates [4, 5, 6] or more complex condensation products [7].

We thought it likely that the enolic acetates of the ketones were produced via the formation as intermediates of diacetyl derivatives of the hydrated form of the ketones, which originate when the acetic anhydride is added to the carbonyl group and, as they are unstable in the conditions of the reaction, split off a molecule of acetic acid. The following facts reported in the literature support the conclusion that the reaction of the aldehydes with acetic anhydride follows the same course: 1) When aldehydes are heated with acetic anhydride, we get acetates of the enolic forms of the aldehydes; when the reaction is performed in the cold, we get the respective diacetyl compounds [8]. 2) When the diacetates of the hydrated forms of the aldehydes are heated, they break down into acetates of the enolic forms and acetic acid [9]. By way of an indirect analogy to this type of reaction between acetic anhydride and carbonyl compounds we may cite the synthesis of ethers of the enolic forms of carbonyl compounds by heating their acetals [10] as well as by the action of certain substances that can split off alcohol molecules [11]; it was found that the acetals of the ketones are less stable than those of the aldehydes [12].

In the present research I have endeavored to synthesize the diacetyl derivative of the hydrated form of a ketone and to secure new experimental data on the formation of enolic acetates of ketones. The substance chosen was one of the simplest cyclic ketones, viz: cyclohexanone, which has two equivalent methylene groups adjacent to the carbonyl group, making it possible to produce the enolic forms and eliminating any possibility of the formation of the isomeric enolic acetates.

I reacted cyclohexanone with acetic anhydride under the conditions that are ordinarily employed in synthesizing diacetyl derivatives from the aldehydes, viz: mixing the ketone with an excess of acetic anhydride at room temperature, and adding a minute amount of concentrated sulfuric acid. We succeeded in securing two reaction products: cyclohexenyl-Δ_1-acetate and cyclohexylidene diacetate.

Cyclohexenyl-Δ_1 acetate had been previously synthesized by boiling cyclohexanone with acetic anhydride for 50 hours in the presence of sodium acetate [4]. In 1945 a simpler method was suggested [5] for synthesizing this compound with a 68% yield, involving the heating of cyclohexanone for 4 hours with acetic anhydride in the presence of p-toluenesulfonic acid and driving off the acetic acid produced in the reaction.

In the conditions we employed the yield of the cyclohexenyl acetate totalled about 70% of the theoretical, based on the cyclohexanone used. In view of the simplicity of the reaction we have described, it may be recommended as a convenient method of producing the enolic acetate of cyclohexanone.

Cyclohexylidene diacetate is not described in the literature. It is a colorless liquid with a faint ether odor, which boils at 99-100° (at 5 mm).

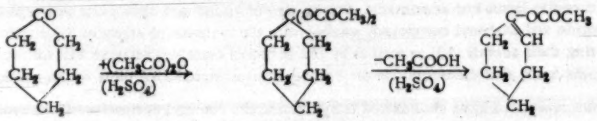
We still had to ascertain whether the formation of the enolic acetate and that of the diacetyl compound were two different processes, independent of each other, or one of these compounds is an intermediate product in the formation of the other. To determine the feasibility of the enol acetate being formed by the direct acylation of the enolic form of cyclohexanone we first investigated the feasibility of acylating the enolic hydroxyl

group under our reaction conditions, using phenol as an example. Our experiment indicated that acylation proceeds readily, a high yield of phenyl acetate being obtained. We still thought that the assumption that the enol acetate was formed by the direct acetylation of the enolic form of cyclohexanone not very likely, inasmuch as the latter form, even if present in equilibrium with the keto form in cyclohexanone, would still exist in a minute quantity; this follows, for example, from the fact that cyclohexanone does not decolorize bromine water rapidly [13].

On the other hand, as we noted above, the addition of acetic anhydride to the carbonyl group takes place very readily in some cases (as in the aldehydes). As I saw it, a more probable assumption, therefore, was that the initial process occurring in the reaction under consideration is the formation of a diacetate, the formation of the enol acetate being a secondary process. This is borne out by the following fact I have discovered: The diacetyl compound is produced only when cyclohexanone reacts with the acetic anhydride for a short time (42 hours). When the reaction lasted a longer time (9 days), no diacetyl compound was secured, the yield of the enol acetate increasing proportionately. Moreover, special tests showed that the enol acetate of cyclohexanone cannot add acetic acid under the prevailing reaction conditions. The enol acetate was mixed with acetic anhydride (three times the molar quantity) and glacial acetic acid (1.5 times the molar quantity), and a few drops of sulfuric acid were added. Three days later, the unchanged enol acetate was recovered from the reaction mixture almost quantitatively. This indicates that the enol acetate is stable under the reaction conditions we are discussing, so that it is hardly an intermediate product during the synthesis of cyclohexylidene diacetate from cyclohexanone.

To bear out our assumption that the diacetyl compound is an intermediate product of the formation of the enol acetate, we investigated the stability of cyclohexylidene diacetate under our reaction conditions. We found that cyclohexylidene diacetate is totally converted into cyclohexenyl-Δ_1 acetate when allowed to stand in the cold with acetic anhydride and a minute amount of sulfuric acid. (See the experimental section for a description of this test).

Hence, our experimental findings support the following schema for the reaction of cyclohexanone with acetic anhydride in the cold in the presence of sulfuric acid.



We shall made an experimental check in the future of whether this schema can be applied to other ketones.

EXPERIMENTAL

1. Synthesis of Cyclohexenyl-Δ_1 Acetate from Cyclohexanone.

Ten drops of concentrated sulfuric acid were added to a mixture of 62.5 g of acetic anhydride and 20 g of cyclohexanone. Heat was liberated (the temperature rising to 37°), and the reaction mixture gradually turned dark crimson. The mixture was allowed to stand at room temperature for 9 days after which it was treated with ice water to decompose the acetic anhydride that had not participated in the reaction and then extracted with ether. The ether solution was washed with a 10% soda solution until its reaction was neutral, and then with water after which it was dried with sodium sulfate. The ether was driven off, and the residue, which contained no cyclohexanone (bisulfate test), was distilled in vacuo; the bulk of the substance was collected in the 58-68° range at 5 mm. The substance had the following constants after redistillation in vacuo:

B.p. 180-181°; n_D^{20} 1.4580; d_4^{20} 1.01103; MR_D 37.83; calculated 38.13.

15.98 mg substance: 40.18 mg CO_2; 12.32 mg H_2O. 14.99 mg substance: 37.79 mg CO_2; 11.54 mg H_2O. Found %: C 68.61, 68.79; H 8.63, 8.61. $C_8H_{12}O_2$. Calculated %: C 68.54; H 8.63.

Saponification number: 381.6. Calculated for cyclohexenyl acetate: 400.2.

The yield of cyclohexenyl-Δ_1 acetate was 20 g, or about 70% of the theoretical.

2. Synthesis of Cyclohexylidene Diacetate from Cyclohexanone.

The quantities of cyclohexanone, acetic anhydride, and sulfuric acid used, and the reaction procedure,

were the same as in Experiment 1. Reaction lasted 42 hours. The reaction mixture was processed with ice water to decompose the acetic anhydride and extracted with ether, and the ether extract was washed with a 10% soda solution. Then the unreacted cyclohexanone was eliminated by using sodium bisulfite. The bisulfite compound weighed 23 g. The residue was washed with soda and then with water and dried, the ether was driven off, and the residue was fractionated in vacuo. Double distillation yielded two products:

1) 10.5 g of a substance with a b.p. of 62-72° (at 5 mm) – cyclohexenyl-Δ_1 acetate.

2) 4.5 g of a product with a b.p. of 98-102° (at 5 mm); several redistillations in vacuo of the product yielded a substance that was a colorless liquid with a faint ether odor:

B.p. 99-100° (at 5 mm); n_D^{20} 1.4475; d_4^{20} 1.0749; MR_D 49.81; calculated 49.49.

15.50 mg substance: 34.31 mg CO_2; 11.29 mg H_2O. 14.80 mg substance: 32.74 mg CO_2; 10.84 mg H_2O. Found %: C 60.40, 60.37; H 8.15, 8.20. $C_{10}H_{16}O_4$. Calculated %: C 59.98; H 8.05.

Saponification number: 550. 3. Calculated for cyclohexylidene diacetate: 560.4.

Conversion of cyclohexylidene diacetate into cyclohexenyl-Δ_1 acetate. Two drops of concentrated sulfuric acid were added to a mixture of 3.5 g of freshly distilled cyclohexylidene diacetate and 5.5 g of acetic anhydride. No heat was liberated; the reaction mixture turned red at once, taking on a dark-crimson color within 1-2 hours. The mixture was allowed to stand for 6 days. Its processing was the same as in Experiment 1. The residue left after the ether had been driven off distilled nearly completely at 60-62° (at 4 mm). When the substance was distilled at atmospheric pressure, all of it passed over at 175-180° and had the ethereal odor that was characteristic of cyclohexenyl-Δ_1 acetate. Its saponification number was 405.3. The number calculated for cyclohexenyl acetate was 400.2

SUMMARY

1. It has been found that when cyclohexanone is reacted in the cold with acetic anhydride and a minute quantity of concentrated sulfuric acid, cyclohexenyl-Δ_1 acetate is produced, the yield being 70% of the theoretical.

2. It has been shown that when cyclohexanone is reacted with acetic anhydride in the cold for a short time in the presence of sulfuric acid, cyclohexylidene diacetate, which is not described in the literature, is produced in addition to the enol acetate of cyclohexanone.

3. It has been found that under these reaction conditions the cyclohexylidene diacetate is an intermediate product of the formation of the enol acetate of cyclohexanone.

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THE CONDENSATION OF SOME 4-ALKYL SUBSTITUTION DERIVATIVES OF CYCLOHEXANONE WITH ENANTHALDEHYDE

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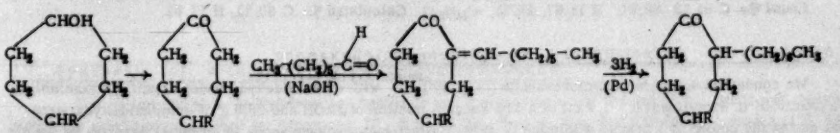
The alkyl and alkenyl substitution derivatives of cyclopentanone and cyclopentenone include several compounds that have a floral odor and are thus of interest to the perfume industry. The best-known compound of this type is jasmone (3-methyl-2-n-pentenylcyclopenten-2-one-1) and its hydrogenation products. Thanks to this, many papers, both research and patent, have dealt with the synthesis of such compounds [1]. The information in the literature on the odor of alkyl substitution derivatives of cyclohexanone is very scanty, however. In one of the patents [2] we found the assertion that 2-heptylidenecyclohexanone can be used as a component of a blend that has the odor of hyacinths.

In view of the fact that alkylphenols and their hydrogenation products – alkyl-cyclohexanols – are quite accessible products by now, we were interested in making use of them to synthesize several alkyl alkilidene hexanones and dialkyl cyclohexanones to secure new fragrant substances.

We took 4-methyl- and 4-tert-butylcyclohexanol as the initial substances. They were converted into the respective cyclohexanones by oxidizing them with dichromate in sulfuric acid, the cyclohexanones then being condensed with enanthaldehyde. The condensation products (which we assume have a semicyclic double-bond structure*) were converted into the respective saturated ketones (dialkyl cyclohexanones) by hydrogenation:



where R = CH_3 or $(CH_3)_3C$.

We condensed the 4-alkyl substitution derivatives of cyclohexane with enanthaldehyde in the presence of a dilute solution of caustic soda (0.5% of the total weight of the reaction mixture) at a temperature of –5° to 0°.

The substances we synthesized were products of the condensation of one molecule of the alkyl cyclohexanone with one molecule of enanthaldehyde, a molecule of water being given off. The presence of a single ethylenic bond in the molecules of the products synthesized was confirmed by the quantity of hydrogen absorbed during its hydrogenation (cf. the experimental section).

When we condensed 4-methylcyclohexanone with enanthaldehyde we secured a liquid product with a faint, but rather pleasant odor. B.p. 134-144° at 4 mm.

The yield of the condensation product was 70% of the theoretical, based on the unreacted enanthaldehyde.

When we condensed 4-tert-butylcyclohexanone with enanthaldehyde, we secured a product that was an oily liquid with hardly any odor. The substance had a b.p. of 152-154° at 5 mm.

The yield of the condensation product was 35% of the theoretical, based on the enanthaldehyde used.

The unsaturated ketones we had synthesized were hydrogenated in alcohol at room temperature with a palladium catalyst (see the experimental section).

* It is not impossible that the double bond is located in the ring in the condensation products (again in an α,β-position to the carbonyl group).

When we hydrogenated 4-methyl-2-heptylidenecyclohexanone, we secured a product that was a colorless liquid with the odor of peaches; b.p. 138-140° at 5 mm; oxime m.p. 64° (with decomposition).

When we hydrogenated 4-tert-butyl-2-heptylidenecyclohexanone, we secured a liquid product that had the odor of fresh greens; b.p. 170-171° at 5 mm; oxime m.p. 62°; semicarbazone m.p. 143-144°; p-nitrophenylhydrazone m.p. 116-117° (with decomposition).

Thus, the unsaturated ketones we synthesized by condensing 4-methyl- and 4-tert-butylcyclohexanone with enanthaldehyde had hardly any odor. The odor was reinforced when the ethylenic bond in these compounds was hydrogenated and its character changed, becoming more fragrant.

EXPERIMENTAL

I. Synthesis of 4-Methyl-2-heptylidenecyclohexanone

1.5 ml of a 31% solution of NaOH and 30 g of enanthaldehyde were added drop by drop, with vigorous mechanical stirring (1.5 hours), to a solution of 46 g of 4-methylcyclohexanone (b.p. 169-170°)* in an equal weight of alcohol, chilled to −10°.

The temperature was kept in the −5° to 0° range. After the alkali and the aldehyde had been added, the mixture was stirred for another hour and a half at 0°. Then the reaction mass was neutralized with 30% acetic acid and agitated with water, the reaction product being extracted with ether and dried with calcined sodium sulfate, and the ether being driven off. Then the unreacted methylcyclohexanone and the enanthaldehyde were driven off in vacuo (40 mm). The residue was distilled with a dephlegmator at a 4 mm vacuum.** The yield of the product, with a b.p. of 140-146° (at 4 mm), was 19.8 g, or 36% of the theoretical, based on the charge of enanthaldehyde (or 70%, based on the aldehyde entering into the reaction).

The product is a colorless oily liquid. Its constants were as follows after double distillation:

B.p. 143-144° at 4 mm; n_D^{19} 1.4788; d_4^{19} 0.90350; MR_D 65.36; calculated 64.20.***

14.94 mg subs.: 44.41 mg CO_2; 15.55 mg H_2O. 14.16 mg subs.: 44.98 mg CO_2; 15.87 mg H_2O.
Found %: C 81.12, 80.97; H 11.67, 11.73. $C_{14}H_{24}O$. Calculated %: C 80.71, H 11.61.

II. Synthesis of 4-Tert-Butyl-2-Heptylidenecyclohexanone.

We condensed 4-tert-butylcyclohexanone (m.p. 49°)**** with enanthaldehyde under conditions resembling those described in Experiment I. 1.5 ml of a 31% aqueous solution of NaOH and 26.5 g of enanthaldehyde were added during the course of 1 hour to a solution of 48 g of 4-tert-butylcyclohexanone in an equal quantity by weight of alcohol, chilled to −10°, the temperature being kept in the −10° to 0° range by external chilling. After all the alkali and aldehyde had been added, the mixture was stirred for another hour at 0°. The condensation product was recovered as described in Experiment I. The yield of the product, with a b.p. of 150-155° (at 1 mm), was 20.3 g, or 35% of the theoretical yield, based in the charged enanthaldehyde. Its constants were as follows after double distillation in vacuo:

B.p. 152-154° (at 1 mm); n_D^{19} 1.4806; d_4^{19} 0.90188; MR_D 78.96; calculated 78.05.***

15.45 mg subs.: 46.24 mg CO_2; 16.84 mg H_2O. 15.23 mg subs.: 45.64 mg CO_2; 16.58 mg H_2O.
Found %: C 81.68, 81.75; H 12.20, 12.18. $C_{17}H_{32}O$. Calculated %: C 81.53; H 12.08.

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* We prepared the 4-methylcyclohexanone by oxidizing 4-methylcyclohexanol with dichromate in sulfuric acid (52% of the theoretical yield).

** The experiment showed that heating with anhydrous oxalic acid, as other authors have done in similar cases [3], was not needed to dehydrate the hydroxy ketone formed initially. Experiments in which the condensation product was heated with oxalic acid yielded the same results. Apparently the hydroxy ketone is readily dehydrated during the distillation of the product in vacuo.

*** The discrepancy between the $MR_{exp.}$ and the $MR_{calc.}$ may be ascribed to the effect of the conjugated double bonds.

**** We prepared the 4-tert-butylcyclohexanone by oxidizing 4-tert-butylcyclohexanol with dichromate, the yield being 44% of the theoretical.

III. Synthesis of 4-Methyl-2-heptylcyclohexanone.

The 4-methyl-2-heptylidenehexanone was hydrogenated in an alcoholic solution by colloidal palladium with vigorous mechanical agitation, using gum arabic as a protective colloid. 8.9 g of the substance absorbed 1040 ml of hydrogen (15°, 738 mm). The calculated quantity for 8.9 g of 4-methyl-2-heptylidenecyclohexanone is 1060 ml of hydrogen. When the reaction was over, the catalyst was filtered out, the alcohol was driven off, and the reaction product was extracted with ether and dried with calcium chloride, after which the ether was driven off and the residue double-distilled in vacuo (5 mm). This yielded 5.8 g of a product with the following constants:

B.p. 138-140° at 5 mm; n_D^{18} 1.4570; d_4^{18} 0.87890; MR_D 65.19; calculated 64.66.

12.12 mg subs.: 35.60 mg CO_2; 13.72 mg H_2O. 12.61 mg subs.: 36.94 mg CO_2; 14.34 mg H_2O.
Found %: C 80.16, 79.94; H 12.69, 12.75. $C_{14}H_{28}O$. Calculated %: C 79.93; H 12.46.

The oxime of 4-methyl-2-heptylcyclohexanone was prepared by boiling a water–alcohol solution of 0.5 g of hydroxylamine hydrochloride, 1 g of sodium acetate, and 1 g of the ketone for 30 minutes on a water bath. It had a constant m.p. of 64° after fourfold recrystallization from alcohol.

13.02 mg subs.: 0.745 ml N_2 (25°, 754 mm). Found %: N 6.50. $C_{14}H_{27}ON$. Calculated %: N 6.21.

The semicarbazone of 4-methyl-2-heptylcyclohexanone was produced by agitating 1 g of the ketone for a long time with a water–alcohol solution of 0.5 g of semicarbazide hydrochloride and 0.5 g of sodium acetate. Its m.p. was constant at 102° after fourfold recrystallization from alcohol.

11.6 mg substance: 1.634 ml N_2 (23.5°, 747 mm). Found %: N 15.92. $C_{15}H_{29}ON_3$.
Calculated %: N 15.72.

The p-nitrophenylhydrazone of 4-methyl-2-heptylcyclohexanone was prepared by heating 1 g of p-nitrophenylhydrazine on a water bath with 1 g of the ketone in glacial acetic acid. It had a m.p. of 114-116° (with decomposition) after fourfold recrystallization from alcohol.

IV. Synthesis of 4-tert-Butyl-2-heptylcyclohexanone.

The 4-tert-butyl-2-heptylidenecyclohexanone was hydrogenated, and the reaction product was recovered under the conditions described for Experiment III. 8.1 g of the substance absorbed 800 ml of hydrogen (17°, 741 mm), the calculated quantity for 8.1 g of 4-tert-butyl-2-heptylidenecyclohexanone being 807 ml.

The synthesized 4-tert-butyl-2-heptylcyclohexanone had the following constants:

B.p. 170-171° at 5 mm; n_D^{17} 1.4662; d_4^{17} 0.88856; MR_D 78.71; calculated 78.52.

14.50 mg subs.: 42.83 mg CO_2; 16.54 mg H_2O. 13.90 mg subs.: 41.01 mg CO_2; 15.72 mg H_2O.
Found %: C 80.60, 80.50; H 12.78, 12.67. $C_{17}H_{32}O$. Calculated %: C 80.88; H 12.78.

The oxime of 4-tert-butyl-2-heptylcyclohexanone was prepared as in Experiment III. Its m.p. was 62° after triple recrystallization from alcohol.

The semicarbazone of 4-tert-butyl-2-heptylcyclohexanone was prepared as in Experiment III. M.p. 143-144° (from alcohol).

12.82 mg subs.: 1.525 ml N_2 (25°, 747 mm). 12.01 mg subs.: 1.463 ml N_2 (27°, 747 mm).
Found %: N 13.37, 13.60. $C_{18}H_{35}ON_3$. Calculated %: N 13.57.

The p-nitrophenylhydrazone of 4-tert-butyl-2-heptylcyclohexanone had a m.p. of 116-117° (with decomposition).

SUMMARY

1. 4-Methyl-2-heptylidenecyclohexanone and 4-tert-butyl-2-heptylidenecyclohexanone, not described previously in the literature, have been synthesized by condensing 4-methyl- and 4-tert-butylcyclohexanone with enanthaldehyde.

2. The synthesized compounds were converted by catalytic hydrogation into 4-methyl-2-heptylcyclohexanone and 4-tert-butyl-2-heptylcyclohexanone, likewise not described previously in the literature. The latter were identified via their oximes, semicarbazones, and p-nitrophenylhydrazones.

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SYNTHESIS AND INVESTIGATION OF 2-PHENYLPENTANOL-2-ONE-3

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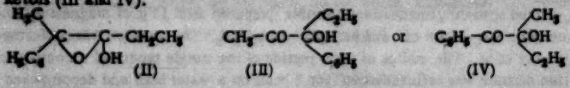
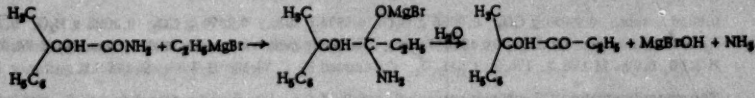
Of the medicinals, absolutely no work has been done on the α-ketols, with the sole exception of the fructoses. The research workers who synthesized these chemical compounds, which are so highly interesting for an understanding of the nature of the sugars, were uninterested in testing their pharmaceutical properties. And yet, if we look into the individual groups in the α-ketols, we may assume that the presence of hydroxyl and ketonic groups greatly favor the origin of hypnotic properties in these substances. Obviously, the radicals linked to the α-hydroxy carbonyl group also play an important part. The presence of a carbonyl group in methyl phenyl, ethyl phenyl, propyl phenyl, and diphenyl ketones, for instance, is responsible for the market soporific action of these compounds, as has also been observed in ketones with aliphatic radicals (methylethyl, . . diethyl, and propyl ketones) [1]. It may also be assumed that if the halogenated hydroxy ketones have no irritating properties, they might also be interesting subjects for research.

The first tertiary α-ketol whose action we tested on animals was 2-phenylpentanol-2-one-3 (I). This ketol is interesting because its α-hydroxy ketone group is linked, one the one hand, to an ethyl radical, the soporific and anesthetic action of which has been confirmed in several examples (ethyl alcohol, diethyl ether, diethylbarbituric acid, and the like), and, on the other, to methyl and phenyl groups, whose hypnotic effects are also commented on in the literature (acetophenone, Luminal, etc.). Synthesizing this compound, we also bore in mind the possibility that it might exist as an α-alcohol ether (II) and the possibility that the alcohol ether or ketol may be isomerized to isomeric ketols (III and IV).



(II) (III) or (IV)

We proposed to synthesize 2-phenylpentanol-2-one-3 by starting either from acetophenone cyanohydrin and ethylmagnesium bromide or from atrolactamide and the same Grignard compound. We were unable to synthesize the ketol from acetophenone cyanohydrin and ethylmagnesium bromide, obtaining 2-phenylbutanol-2 instead of the expected ketol. A 25% yield of the ketol was obtained when we reacted atrolactamide with ethylmagnesium bromide.



The reaction is actually more complicated, since we have to allow for the action of the hydroxyl group, which decomposes the organomagnesium coordination compound. We therefore used 3 moles of ethylmagnesium bromide per mole of atrolactamide for the reaction. The synthesized ketol had a pleasant aromatic fragrance and a boiling point of 131-132° (10 mm). The structure of the ketol was established by oxidizing it with chromic anhydride in the presence of potassium bisulfate. This yielded acetophenone, identified via its semicarbazone, with a m.p. of 201-202°, and propionic acid, identified via its silver salt. We also investigated the ketol's behavior with a methanol solution of HCl, in order to determine whether an α-alcohol – ether structure was present, but we were unable to secure a methyl lactolide: the action of phenyl isocyanate yielded a phenylurethane with a m.p. of 182-183°. When we tried to isomerize 2-phenylpentanol-2-one-3 by heating it in a sealed tube to 120° with alcohol in the presence of sulfuric acid, the ketol was dehydrated, yielding 2-phenylpenten-1-one-3. The presence of the latter was established by the products of oxidation with potassium permanganate: we found benzoic and propionic acids, plus, apparently, formic acid, as the silver salts turned very black.

The pharmacological testing of 2-phenylpentanol-2-one-3 on mice, carried out under the guidance of N.A. Kharasov (to whom we are indebted), indicated that the ketol exhibited a narcotic effect resembling that of amylene hydrate, but about five times as powerful; the phenylurethane, on the other hand, was inactive.

EXPERIMENTAL

Reaction of acetophenone cyanohydrin with ethylmagnesium bromide. A solution of 109 g of ethyl bromide in twice the volume of ether was gradually added from a dropping funnel to 24 g of magnesium in ether; a solution of 205 g of acetophenone cyanohydrin in twice its volume of ether was added, with chilling to 0°, to the resulting ethylmagnesium bromide. The reaction involved the evolution of considerable heat, a dark-gray organomagnesium coordination compound that was ether-insoluble and was stirred with difficulty by the stirrer being produced as the acetophenone cyanohydrin was added. After all the acetophenone cyanohydrin had been added, the reaction mixture was refluxed for two hours at 30-35° on a water bath and then decomposed with a 10% solution of ammonium chloride after it had cooled. After the ether solution had been washed with a 2% solution of hydrochloric acid and the ether had been driven off, the residue was fractionated at 10 mm pressure. This yielded 13 g of a 80-92° fraction and 199 g of a 93-105° fraction. Redistillation of the 93-105° fraction at 10 mm yielded: 2 g at 89-92° and 194 g at 100-101°. We analyzed the fraction with a b.p. of 100-101° at 10 mm.

d_4^1 0.9963; d_4^{20} 0.9850, n_d^{20} 1.51569; MR_d 45.97; calculated 46.12.

0.0938 g subs.: 0.2745 g CO_2; 0.0787 g H_2O. 0.0892 g subs.: 0.2603 g CO_2; 0.0749 g H_2O. 0.1928 g subs.: 15.7943 g benzene; Δt 0.43°. 0.2004 g subs.: 17.4128 g benzene: Δt 0.40°. Found %: C 79.81, 79.59; H 9.38, 9.39; M 145, 147. $C_{10}H_{14}O$. Calculated %: C 80.00; H 9.33; M 150.

The substance is a transparent, colorless liquid with a putrid odor. The action of phenyl isocyanate upon it produced a phenylurethane, whose m.p. was 161° after recrystallization from alcohol.

0.1523 g subs.: 6.70 ml N_2 (11°, 752 mm). 0.1411 g subs.: 615 ml N_2 (12°, 754 mm).
Found %: N 5.20, 5.15. $C_{17}H_{19}O_2N$. Calculated %: N 5.20.

The analytical data indicate that the reaction produced 2-phenylbutanol-2. It is evident that acetophenonecyanohydrin is decomposed by ethylmagnesium bromide, producing acetophenone, which reacted with the Grignard reagent. The properties of the resulting carbinol agreed with those given in the literature [2].

2-Phenylpentanol-2-one-3. 30 g of atrolactamide, with a m.p. of 101-102° synthesized by the Ruzicka and Staudinger method [3] was reacted with ethylmagnesium bromide prepared with 13 g of magnesium and 59 g of ethyl bromide in ether. Then the ether was driven off, and benzene was added. The reaction was performed at 75-80°, the amide being added in the dry state. The adding of each portion of the amide produced a considerable rise in temperature. Then the reaction mixture was refluxed at 80° for 3 hours on a water bath and decomposed the next day with water and a 10% solution of ammonium chloride. The reaction product was extracted with ether, which was then driven off after the extract had been dried over sodium sulfate; driving off the benzene in vacuo yielded 7.5 g of a substance with a b.p. of 131-132° at 10 mm.

d_4^1 0.9771; d_{15}^{20} 0.9700; n_d^{20} 1.39822; MR_d 44.33; calculated 44.87.

0.0916 g subs.: 0.2486 g CO_2; 0.0655 g H_2O. 0.0874 g subs.: 0.2372 g CO_2; 0.0625 g H_2O. 0.1412 g subs.: 17.0854 g benzene: Δt 0.27°. 0.1395 g subs.: 15.0606 g benzene; Δt 0.024°. Found %: C 74.02, 74.01; H 8.00, 8.00; M 176.3, 175.8. $C_{11}H_{14}O_2$. Calculated %: C 74.16; H 7.87; M 178.11.

The phenylurethane of 2-phenylpentanol-2-one-3. 1.8 g of 2-phenylpentanol-2-one-3, with a b.p. of 131-132° at 10 mm was mixed with 1.2 g of phenylisocyanate and heated to 40-50° in a sealed tube for 30 minutes. The reaction product was washed on a Buchner funnel with a mixture of petroleum and diethyl ethers, and then with water, dried in a vacuum desiccator, and recrystallized from alcohol; m.p. 182-183°.

0.2082 g subs.: 8.20 ml N_2 (15°, 758 mm). 0.2283 g subs.: 8.80 ml N_2 (16°, 756 mm).
Found %: N 4.65, 4.53. $C_{18}H_{19}O_2N$. Calculated %: N 4.71.

Oxidizing the ketol. 3 g of the ketol was oxidized with 3.15 g of chromic anhydride in the presence of 6.5 g of potassium bisulfate and 36 g of water, the reaction product being distilled with steam. The distillate was neutralized with potash, and then a neutral product with the odor of acetophenone was driven off and collected in a semicarbazide solution. The semicarbazone precipitate had a m.p. of 201-202° after recrystallization from alcohol; its mixed melting point with the semicarbazone of acetophenone exhibited no depression.

0.0808 g substance: 15.75 ml N_2 (12.5°, 768.8 mm). 0.1032 g substance: 20.30 ml N_2 (14°, 767 mm).
Found %: N 23.00, 24.32. $C_9H_{11}ON_3$. Calculated %: N 23.73.

After the potash solution had been acidulated with dilute sulfuric acid, the acid products were driven off with steam; the distillate was heated and saturated with freshly prepared silver carbonate, the silver salts of the acids being filtered out and fractionally crystallized. The individual fractions contained the following amounts of silver after they had been dried in the vacuum desiccator:

0.0694 g subs.: 0.0414 g Ag. 0.0721 g subs.: 0.0430 g Ag.
Found %: Ag 56.95 59.64. $C_3H_5O_2Ag$. Calculated %: Ag 59.67.

The formation of acetophenone and propionic acid when the ketol was oxidized identified the structure of the ketol as that of 2-phenylpentanol-2-one-3.

2-Phenylpenten-1-one-3. The 2-phenylpentanol-2-one-3 was heated to 120° in a sealed tube with sulfuric acid in order to determine its resistance to acid agents and its ability to enter into the isomeric transformations described by Academician A.E.Favorsky and his pupils for several other α-ketols [4]. We used 6.5 g of the ketol, with a b.p. of 131-132° at 10 mm, 20 g of ethyl alcohol, and 5 drops of conc.sulfuric acid. After the reaction mixture had been heated for 8 hours, it was neutralized with anhydrous barium carbonate, the alcohol being driven off from the filtrate in vacuo, and the residue being distilled. This yielded 3.5 g of a substance with a b.p. of 117-118° at 10 mm, which decolorized bromine and potassium permanganate solutions. Because of the small quantity available, the substance was oxidized with potassium permanganate without further detailed identification.

The 3.5 g of the substance was oxidized by 207.5 g of a 2% solution of potassium permanganate; the filtrate was acidulated with sulfuric acid and then fractionated. The distillates were heated and saturated with freshly prepared silver carbonate and then crystallized in a vacuum desiccator after having been boiled for a long time and refiltered (owing to the precipitation of metallic silver).

Fraction 1: 1.04 g; 0.1002 g subs.: 0.0470 g Ag. 0.1064 g subs.: 0.0481 g Ag.

Fraction 2: 1.02 g; 0.0947 g subs.: 0.0465 g Ag. 0.1233 g subs.: 0.0617 g Ag.

Fraction 3: 0.93 g; 0.1043 g subs.: 0.0610 g Ag. 0.1112 g subs.: 0.0650 g Ag.

Found %: Ag 46.92, 47.28, 49.11, 50.05, 59.60, 59.23. $C_3H_5O_2Ag$.

Calculated %: Ag 47.16. $C_3H_5O_2Ag$. Calculated %: Ag 59.67.

SUMMARY

1. When acetophenone cyanohydrin is reacted with ethylmagnesium bromide, 2-phenylbutanol-2 is produced.

2. The reaction of atrolactamide with ethylmagnesium bromide in benzene yields 2-phenylpentanol-2-one-3.

3. When 2-phenylpentanol-2-one-3 is heated to 120° with sulfuric acid and alcohol, the hydroxy ketone is dehydrated yielding 2-phenylpenten-1-one-3.

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THE ACTION OF NITROUS ACID UPON 2-METHOXYDIMETHYLANILINE

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Some substitution derivatives of dimethylaniline yield the corresponding mononitro derivatives when reacted with nitrous acid in aqueous solution. For instance, 4-methyldimethylaniline yields 3-nitro-4-dimethylaminotoluene [1,2], while 4-methoxy- [3], 4-chloro- [4,5,6], and 4-bromodimethylaniline [7,8] react similarly. This reaction is usually complicated by the formation of nitroaryl alkyl nitrosamines [1,2,3,8]

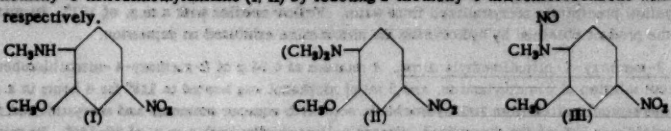
Grimaux and Lefevre [9] investigated the action of nitrous acid upon 2-methoxydimethylaniline, finding that the sole reaction product was 2-methoxy-4-nitrodimethylaniline. But when we repeated their work, we always secured a mixture of two substances, which could be readily separated by processing with dilute hydrochloric acid.

The substance that is soluble in the acid at room temperature was precipitated from the solution by aqueous ammonia and crystallized from alcohol, being recovered as orange-yellow needles with a m.p. of 99-100°, which is the figure given by Grimaux and Lefevre [9] for 2-methoxy-4-nitrodimethylaniline.

The acid-insoluble residue was crystallized from alcohol, yielding slightly yellowish minute needles with a m.p. of 135-136°, which exhibited a pronounced Liebermann reaction for nitrosamines.

When the product was heated with 25% hydrochloric acid, it dissolved, giving off nitrogen oxides. Precipitation with ammonia and crystallization from water yielded yellow needles with a m.p. of 102°, which is the melting point of the 2-methoxy-4-nitromethylaniline synthesized by Ingold and Ingold [10] in another way.

In order to establish the structure of the two products, we synthesized 2-methoxy-4-nitromonomethylaniline and 2-methoxy-4-nitrodimethylaniline (I, II) by reacting 2-methoxy-4-nitrochlorobenzene with mono- and dimethylamine, respectively.



We found that the first of these was identical with the product of the hydrolysis of the substance with a m.p. of 135-136°, while the second was the same as the product with a m.p. of 99-100°.

Then, we nitrosated 2-methoxy-4-nitromethylaniline (I) and secured 2-methoxy-4-nitrophenylmethylnitrosamine (III) [11], the properties of which were exactly the same as those of the substance with a m.p. of 135-136° recovered from the reaction product. The same compound is produced by the action of nitrous acid upon 2-methoxy-4-nitrodimethylaniline in an acidic solution.

Thus, the corresponding nitrosamine is produced, in addition to the 4-nitro derivative, when 2-methoxydimethylaniline is reacted with nitrous acid in an aqueous solution, as was the case with other substitution derivatives of dimethylaniline [1,2,3,8].

The formation of the nitrosamines is apparently largely due to the reaction of the resultant nitro product with excess of nitrous acid present in the reaction mixture (cf. [12]).

EXPERIMENTAL

The 2-methoxydimethylaniline was prepared by methylating o-aniline (1 mole) with dimethyl sulfate (3.6 moles) at 20-25° in a slightly alkaline aqueous solution and then decomposing the resultant o-methoxyphenyltrimethylammonium hydroxide by distilling the reaction mass. The yield was 71% of the theoretical (Evans and Williams secured a yield that was only 40% of the theoretical, using a smaller excess of the dimethyl sulfate [13]). A nearly colorless oil with a b.p. of 210-212°.

Reaction of 2-methoxydimethylaniline with nitrous acid [9]. A solution of 45.3 g of sodium nitrite in 2700 ml of water was gradually added, at 15-20°, with stirring, to a solution of 15.1 g of 2-methoxydimethylaniline in 90 g of 33% sulfuric acid, a yellow crystalline precipitate being thrown down. Twelve hours later an excess of aqueous ammonia was added to the reaction mass, and the precipitate was filtered out, washed with water, dried (m.p. 98-107°), and treated 3 or 4 times with 10% hydrochloric acid (in 50-60 ml portions). After each treatment, the insoluble residue was filtered out and washed with 10% hydrochloric acid. The filtrate was combined with the wash waters and alkalinized with aqueous ammonia, the resultant precipitate being filtered out, washed with water, and dried, after which it was crystallized from 75 ml of ethyl alcohol.

The yield was 7.1 g (36.2% of the theoretical). Thin orange-yellow needles with a m.p. of 99-100° (Grimaux and Lefevre [9] give the m.p. as 99°).

Found %: N 14.37, 14.42. $C_9H_{12}O_3N_2$. Calculated %: N 14.28.

The residue left after the reaction product had been treated with 10% hydrochloric acid was crystallized from ethyl alcohol. Slightly yellowish needles with a m.p. of 135-136° (Best [11] gives 138° as the m.p. of 2-methoxy-4-nitrophenylmethylnitroamine). The yield was 8.2 g (38.8% of the theoretical).

Found %: N 20.00, 20.06. $C_8H_9O_4N_3$. Calculated %: N 19.91.

A mixture of 1.05 g of the product with a m.p. of 135-136° and 10.5 ml of 25% hydrochloric acid was refluxed for 1 hour. The substance dissolved rapidly, nitrogen oxides being given off. An excess of aqueous ammonia was poured into the solution, a yellow precipitate (weighing 0.86 g; m.p. 95-98°) that was recrystallized from water settling out.

Yellow needles with a m.p. of 102° (Ingold and Ingold [10] give the m.p. of 2-methoxy-4-nitromethylaniline as 101-102°).

Found %: N 15.47. $C_8H_{10}O_3N_2$. Calculated %: N 15.35.

Synthesis of 2-methoxy-4-nitromethylaniline. 0.94 g of 2-methoxy-4-nitrochlorobenzene was heated to 110° for 4 hours in a sealed tube with 2.6 g of a 25% aqueous solution of methylamine and 3 ml of methanol. The contents of the tube were then processed with 10% hydrochloric acid and filtered, the filtrate being alkalinized with ammonia, and the yellow precipitate recrystallized from water. Yellow needles with a m.p. of 101°. Its mixed melting point with the product obtained by hydrolyzing the nitrosamine exhibited no depression.

Synthesis of 2-methoxy-4-nitrodimethylaniline. A mixture of 0.94 g of 2-methoxy-4-nitrochlorobenzene, 2.6 g of a 33% aqueous solution of dimethylamine, and 3 ml of methanol was heated to 110° for 4 hours in a sealed tube. The product was reprecipitated from 10% hydrochloric acid with aqueous ammonia and recrystallized from ethyl alcohol. The yield was 97% of the theoretical. Orange-yellow needles with a m.p. of 99-100°. Its mixed melting point with the product recovered from the reaction mixture when 2-methoxydimethylaniline was reacted with nitrous acid exhibited no depression.

Reaction of 2-methoxy-4-nitromonomethyl- and dimethylaniline with nitrous acid. 0.19 g of sodium nitrite as a 10% aqueous solution was added at 15° to a solution of 0.46 g of 2-methoxy-4-nitromethylaniline in 6 ml of 15% hydrochloric acid, throwing down an abundant yellowish precipitate. The yield totaled 85% of the theoretical after recrystallization from ethyl alcohol. Pale-yellow needles with a m.p. of 135.5°.

Under the same conditions, 2-methoxy-4-nitrodimethylaniline yielded a slightly yellowish product, the yield being 30% of the theoretical. M.p. 135-136°.

The mixed melting point of these two substances, as well as of each of them separately with the product having a m.p. of 135-136° that was synthesized by reacting 2-methoxydimethylaniline with nitrous acid, exhibited no depression.

SUMMARY

1. It has been shown that, contrary to the data in the literature, the reaction of nitrous acid in aqueous solution upon 2-methoxydimethylaniline yields a substantial quantity of 2-methoxy-4-nitrophenylmethylnitrosamine in addition to 2-methoxy-4-nitrodimethylaniline.

2. The 2-methoxy-4-nitromono- and dimethylanilines have been synthesized from 2-methoxy-4-nitrochlorobenzene and the mono- and dimethylamines.

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XLVI. THE POLYMERIZATION OF 2,6-DIMETHYL-4-TERT-BUTYLSTYRENE

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Consideration of the problem of how the polymerizability of unsaturated compounds is governed by their structure led one of the present authors to conclude that the principal factor determining whether this ability is present or not is the number of substituents attached to the carbon atoms linked by a double bond, and their dimensions [1]. These stereochemical factors are particularly important in derivatives of ethylene that contain 4, 3, or 2 substituents attached to the ethylenic carbon atoms [2]. As we know, most of these substances cannot be polymerized. The exceptions are those in which these substituents are small, such as tetrafluoroethylene, vinylidene chloride, isobutylene, etc. When the substituent is fairly large, such as a phenylgroup, noneofthe substituted ethylenes, beginning with diphenylethylene, is polymerizable. Diphenylethylene can only be started on the polymerization road, which breaks off at the dimer stage, due to these same stereochemical factors [3]. Only monophenylethylene—styrene—turns out to be a very readily polymerizable substance.

We were therefore interested in seeing whether the presence of other substituents in the styrene molecule besides the phenyl group might not lead to a loss of polymerizability. The monosubstituted orthostyrenes described in the literature polymerize readily, as has been established in the cases of o-fluorostyrene [4], o-chlorostyrene [5], o-bromostyrene [6], o-methylstyrene [7], o-methoxystyrene [4], and o-aminostyrene [6]; this is also true of the disubstitution derivatives that have one of the substituents at the ortho position, such as 2,3-, 2,4-, and 2,5-dichlorostyrene [8], 2,4- and 2,5-dimethylstyrene [9], 2-methyl-4-methoxy-5-isopropylstyrene [10], and α-vinylnaphthalene [7]. Of the ortho disubstitution derivatives of styrene, only one is known: 2,6-dichlorostyrene, which is polymerized when irradiated by ultraviolet rays [8]. We tried to discover whether the presence of two methyl groups in the ortho position to the vinyl group would impede polymerization. With this in mind we synthesized 2,6-dimethyl-4-tert-dibutylstyrene and investigated its polymerizability.

The starting product for the synthesis was 2,6-dimethyl-4-tert-butylacetophenone, which was reduced to 2,6-dimethyl-4-tert-butylphenylmethylcarbinol, which in turn was converted into the desired 2,6-dimethyl-4-tert-butylstyrene by dehydration. The 2,6-dimethyl-4-tert-butylacetophenone was reduced by boiling for 2.5 hours with aluminum isopropylate, and then slowly driving off the isopropyl alcohol and the acetone. Toward the end of this latter procedure the carbinol was also dehydrated, and we got the desired styrene all at once. Distillation yielded a product with a b.p. of 74-76° at 3 mm. The yield of 2,6-dimethyl-4-tert-butylstyrene was 36% of the theoretical.

The resultant product was processed variously to convert it into a polymer. It was heated in the pure state, as well as with benzoyl peroxide added; it was also exposed to the action of direct sunlight, and, lastly, it was treated with such catalysts as boron fluoride or aluminum chloride while chilled to −15° to −25°. It was found that 2,6-dimethyl-4-tert-butylstyrene is polymerized neither thermally nor photochemically, nor is it changed when heated with benzoyl peroxide; only after 250 hours of heating to 200° is a low-molecular polymer produced. Thus, it is practically incapable of radical polymerization, which is initiated, as we know, by compounds or by influences of an energy nature, leading, to the formation of free radicals, as has been demonstrated by Medvedev [11] and others. The use of catalysts was found to be more effective, producing ionic polymerization [12]. Polymerization occurs readily in the presence of boron fluoride or aluminum chloride in a carbon tetrachloride solution chilled below −15°, resulting in the formation of a polymer of 2,6-dimethyl-4-tert-butylstyrene, which is a glasslike product or a white powder, with a m.p. of 180-190.

Hence, 2,6-dimethyl-4-tert-butylstyrene is an example of a substituted styrene that has lost its radical polymerizability almost completely. As we know, styrene itself is a compound that is polymerizable both by the radical and the ionic mechanism, wherein it differs from most other vinyl derivatives, which are usually polymerized in only one way, depending on their structure, as indicated in the table.

Mechanism of polymerizing the monomers		
Radical	Ionic	Hydrolytic
$CH_2=CHCl$	$CH_2=C(CH_3)_2$	CH_2O
$CH_2=CCl_2$	$CH_2=CHOR$	CH_2-CH_2 (O)
$CH_2=CHCOOR$	$CH_2=C(CH_3)C_6H_5$	$NH(CH_2)_5CO$
$CH_2=CHC_6H_5$	$CH_2=CHC_6H_5$	

Inspection of the table indicates that the introduction of two methyl groups into the phenyl ring of styrene at the ortho position to the vinyl group produces the same result as the introduction of one methyl group in the α-position to the vinyl group. This idea can be confirmed by comparing the 2,6-dimethyl-4-tert-butylstyrene we have synthesized with α-methylstyrene: both of these compounds lost the inherent radical polymerizability of the unsubstituted styrene. The reason for this, no doubt, resides in stereochemical relationships. The introduction of these methyl groups sets up steric hindrances to the polymerization process of polymerization, is unable to overcome in the radical schema. But these steric hindrances do not interfere with the polymerization process when the latter proceeds along ionic lines, as we have seen in the two styrenes mentioned above. It is not impossible that the reason for this difference is related to the well-known fact that the radius of action of polar and nonpolar forces varies differently with a change in distance, for the nonpolar forces grow weaker with distance as $1/r^6$, where r is the distance between the centers of attraction, while the polar forces do so only as $1/r^3$. We may, therefore, say that the intensity of interaction will greatly differ for any given atoms at any given distance, depending upon whether they are polar or not. In the former case, when polar interaction forces are present (as is the case in ionic polymerization, where ions of opposite charge unite), the attractive forces will operate over a much greater distance than in the second case, when nonpolar interaction forces are present (as in radical polymerization).

EXPERIMENTAL

2,6-Dimethyl-4-tert-butylstyrene. 300 ml of absolute isopropyl alcohol, 25 g of amalgamated aluminum, and 0.5 g of mercuric chloride were placed in a 0.5-liter round-bottomed flask fitted with a reflux condenser. Then the flask was heated to boiling on a water bath, and 2 ml of carbon tetrachloride was added. A violent reaction set in almost at once, so that the flask had to be chilled with cold water until the reaction slowed down. Then the flask was heated on a boiling water bath until all the aluminum had dissolved. When it had dissolved, 130 g of 2,6-dimethyl-4-tert-butylacetophenone was added, and the reaction mixture was boiled for 2.5 hours on a water bath. After this time had elapsed, a straight condenser was fitted on, replacing the reflux one, and the isopropyl alcohol and the acetone were slowly driven off, first on a water bath, and toward the end on a screen. The reaction mass foamed strongly after the isopropyl alcohol had been driven off, the synthesized 2,6-dimethyl-4-tert-butylphenylmethylcarbinol being dehydrated. The flask was cooled, and the resultant porous, brittle mass was processed with water and with dilute hydrochloric acid. The oil was separated in a separatory funnel, washed several times with water, dried with potash, and distilled in vacuo. Most of the product distilled between 74° and 76° at 3 mm. The yield was 42.3 g, or 36.3% of the theoretical.

2,6-Dimethyl-4-tert-butylstyrene is a colorless oil with the odor of turpentine. It is freely soluble in benzene, dichloroethane, carbon tetrachloride, alcohol, and other organic solvents, and insoluble in water.

d_4^{20} 0.8959; n_D^{20} 1.5220; MR_D 64.42; calculated 64.20.

10.7 mg subs.: 35.24 mg CO_2; 9.61 mg H_2O. 13.46 mg subs.: 44.43 mg CO_2; 12.26 mg H_2O.
Found %: C 89.88, 90.08; H 10.04, 10.19. $C_{14}H_{20}$. Calculated %: C 89.32; H 10.70.

Polymerization of 2,6-dimethyl-4-tert-butylstyrene. 2 g of 2,6-dimethyl-4-tert-butylstyrene was dissolved in 10 g of carbon tetrachloride and chilled to −15°, after which 0.2 ml of a 10% solution of aluminum chloride in nitrobenzene was added or else boron fluoride (1% by weight) was passed through for a short time. Then the mixture was allowed to stand for a few hours, after which it was washed with dilute hydrochloric acid to remove the aluminum chloride, washed with water, and dried with calcium chloride, and the solvent was driven off. This yielded a polymer of 2,6-dimethyl-4-tert-butylstyrene as a colorless hyaline product that fused in the 180-190° range. Its molecular weight, determined by the viscosity of a benzene solution, was 13,500 when aluminum chloride was used and 29,900 when we used boron fluoride.

SUMMARY

1. 2,6-Dimethyl-4-tert-butylstyrene has been synthesized, and its polymerizability has been investigated.

2. It has been found that 2,6-dimethyl-4-tert-butylstyrene is not polymerized by heating it with benzoyl peroxide or by irradiation, while it is readily polymerized in the presence of aluminum chloride or boron fluoride.

3. The problem of the influence of substituents in the ortho position upon the polymerizability of a disubstitution derivative of styrene is discussed, and an explanation is provided for its ionic polymerizability.

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XLVII. THE MECHANISM INVOLVED IN CHAIN GROWTH AND THE REASONS FOR ITS STOPPAGE DURING A POLYESTERIFICATION REACTION [1]

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The mechanism involved in polyesterification and its kinetics have been the subject of several researches, the foundation of which was laid by the classic researches of N.A.Menshutkin, who made a study of the kinetics of the polyesterification reaction as far back as 1881 in his investigation of the reaction of ethylene glycol with succinic acid [2].

Maksorov [3] thoroughly investigated the kinetics of the reaction between ethylene glycol and phthalic anhydride. Subsequently, Kienle and Hovey investigated the reaction of phthalic anhydride with glycerol and ethylene glycol [4]. The latter reaction was studied by Kogan, who found that it was a second-order reaction [5]. The same conclusion was reached by Altman and Kedrinsky from their investigation of the reaction of ethylene glycol and propylene glycol with phthalic anhydride [6]. We find different conclusions reached by Flory, who believes that the reaction of glycols with dicarboxylic acids is of the third order [7]. It should be noted, however, that the experimental findings on which he based his conclusion are not too reliable [8]. A study of various questions related to the mechanism of the polyesterification process and its kinetics was made by Korshak, Rafikov, and Chelnokova; they investigated the reaction of ethylene glycol and of decamethylene glycol with adipic and sebacic acids [9, 10, 11, 12]. As a result of these investigations they calculated the activation energy of the polyesterification reaction, which was found to be 12,000 cal/mole [8]. They also determined the kinetics of this process in the reaction of adipic acid with ethyleneglycol and decamethylene glycol, finding that this was a second-order reaction [8]. Fractionation of the polyesters indicated that they were comparatively homogeneous substances, not containing fractions whose molecular weight differed by more than 20% from the mean molecular weight of the given sample, a consequence of "condensed polymerization equilibrium," which limits the growth of the polyester chains [9,10]. They proposed that the "coefficient of polydispersion," representing the ratio of the gravimetric and numerical molecular weights for any given sample of a polyester [11], be utilized to characterize the fractional composition. They also worked out a method of determining the molecular weights of polyesters from their terminal groups [12].

The problem of the causes of the stoppage of chain growth in the condensed polymerization of dicarboxylic acids with glycols was also examined, it being shown that the existence of destructive reactions in this process, established by one of the present authors together with Golubev [13], ought to result in the formation of a comparatively monodisperse product [14, 15, 16]. The problem of the mechanism involved in polyester chain growth in the various stages of the process still remained unsolved, nor was there any experimental basis for the explanation previously advanced for the reasons underlying the stoppage of chain growth in the polyesterification reaction [14].

The present research was undertaken to obtain data for shedding light on these problems. We chose as the object of our investigation the condensed polymerization of hexamethylene glycol with sebacic acid. Since these starting products were non-volatile compounds with high boiling points, we did not have to worry about their evaporation during the reaction. We thus eliminated any danger of violating the equivalent proportions of the initial substances, which is an extremely important factor determining the upper limit of the polyester's molecular weight [19], as has been demonstrated by one of the present authors in association with Golubev [13, 17] and with Rafikov [18].

EXPERIMENTAL PROCEDURE

The polyesterification of hexamethylene glycol with sebacic acid was carried out at 200°. A current of nitrogen, freed of any oxygen by passing it through an alkaline solution of pyrogallol, then through sulfuric acid, and finally through a layer of the molten polyester heated to 200°, was passed through the reaction vessel continuously. The initial substances were taken in strictly equivalent quantities. In some tests we employed a vacuum of

TABLE 1

Test No.	Duration of reaction, hours	Reaction temperature and conditions	Yield: Polyester (% by weight of total reaction mass)	Yield: Low-molecular polyester (% by wt)	% of unreacted acid (by wt. of original amount)	Characteristics of the polyester: Ml of 0.02 N alkali solution used in determining groups: Hydroxyl	Ml of 0.02 N alkali solution used in determining groups: Carboxyl	Molecular weight by terminal-group method	Specific viscosity	Molecular weight by viscosity method
1	0.5	200°	6.1	60.9	32.9	50.7	50.5	899	0.026	885
2	1.5		46.8	37.1	10.1	41.3	40.7	1219	0.035	1192
3	2.5		82.3	13.3	2.7	29.8	29.2	1694	0.052	1271
4	3.5		85.6	11.9	1.5	24.1	24.2	2070	0.061	2028
5	4.5		89.3	8.5	1.4	22.8	22.6	2202	0.069	2350
6	5.5		91.3	6.7	1.2	19.5	19.4	2570	0.076	2589
7	6.0		91.8	6.2	1.2	19.5	19.4	2570	0.077	2623
8	7.0		93.0	5.8	0.72	18.3	18.2	2739	0.085	2896
9	9.0		96.0	4.0	–	18.1	18.0	2770	0.10	3507
10	10		96.1	3.9	–	17.8	17.6	2892	0.10	3507
11	1.5		96.1	3.9	–	16.9	16.9	2967	0.10	3507
12	2.0	200° in	96.1	3.9	–	16.0	16.0	3125	0.105	3577
13	4.0	vacuo,	97.3	2.7	–	16.1	16.0	3112	0.107	3665
14	6.0	1.5-2 mm	97.6	2.4	–	16.2	16.0	3105	0.109	3717
15	8.0	Hg	98.6	1.4	–	16.2	16.0	3105	0.11	3747
16	10		99.07	0.93	–	16.2	16.0	3105	0.116	3952
17	2.0	260° in vacuo, 1.5-2 mm Hg	99.64	0.36	–	14.2	14.0	3545	0.16	5451

1.5 to 2 mm. Samples of the reaction mass were taken from the reaction vessel at intervals and subjected to thorough analysis. In these samples we determined the terminal groups, the viscosity of an 0.5% solution in benzene, the percentage of the unreacted initial substances, and the precentage of low-molecular reaction products.

Determination of the initial products and of the low-molecular polyesters. This determination was based on the circumstance that the polyester of hexamethylene glycol and sebacic acid is insoluble in diethyl ether, whereas hexamethylene glycol and sebacic acid are both freely soluble in that ether. We first ran blank tests in which weighed samples of the polyester, hexanediol, and the sebacic acid were fused, the resultant mixture being extracted with diethyl ether. The insoluble residue was filtered out, washed with diethyl ether, dried to constant weight, and weighed. The losses of the polyester in these blank tests did not exceed 0.06%. The diethyl ether, which contained the monomers and the low-molecular polyester (with a molecular weight below 800), was filtered free of the insoluble polyester and then distilled off, the residue being dissolved in water. The sebacic acid entered into aqueous solution. The aqueous extract was titrated with a 0.5 N solution of potassium hydroxide. The losses of sebacic acid in the blank tests did not exceed 0.3-0.4%. After the monomers and the low-molecular polymer had been removed, the polyester was analyzed by determining its terminal groups – both carboxylic and hydroxyl – and the viscosity of its 0.5% solution in benzene. The amount of the low-molecular polyester was determined by the method of differences.

Determination of carboxylic groups in the polyester. The number of carboxylic groups was determined by directly titrating a weighed sample of the polyester with a caustic alkali and phenolphthalein. The sample of the polyester (about 0.5 g) was dissolved in 20 ml of a 1:1 chloroform–methanol mixture and titrated with a 0.02 N solution of potassium hydroxide in 60% methanol. The titer of the alkali was established with adipic acid.

Determination of hydroxyl groups. The hydroxyl groups were determined by the Verley method, acetylating the polyester with acetic anhydride in pyridine [20]. A weighed sample of the polyester (about 0.5 g) was placed in a flask fitted with a ground-glass stopper, dissolved in a mixture of pyridine and acetic anhydride, using 120 g of acetic anhydride to 880 g of pyridine, and heated at 80-82° in a water thermostat. A parallel blank test was run under the same conditions. Heating in the thermostat continued for 15 minutes, after which the flask was cooled, and its contents diluted with distilled water and titrated with a 0.05 N solution of potassium hydroxide, using phenolphthalein as an indicator. The molecular weight was determined by the terminal-group method from the results of analysis, using the following formula [21]:

$$M = \frac{100000}{a + b};$$

where a is the number of ml of a 0.02 N solution of potassium hydroxide used to titrate the carboxyl groups, and b is the number of ml of a 0.02 N solution of potassium hydroxide used in determining the hydroxyl groups. Our results are given in Table 1.

EVALUATION OF RESULTS

The results of our investigation of the kinetics of the reaction between hexamethylene glycol and sebacic acid, reproduced in Table 1, indicate that the reactive functional groups are used up fairly rapidly. This is shown more clearly in Figure 1, where we have plotted the kinetics of the change in the percentage of sebacic acid in the reaction mass and in the percentage of the polyester produced with time.

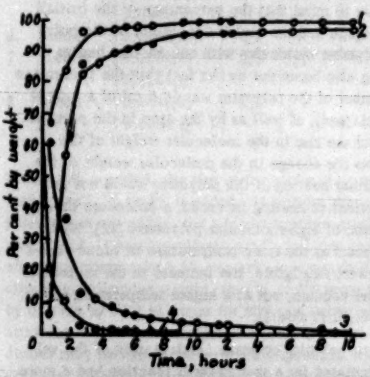

Fig. 1. 1) Change in the percentage of the polyester in the reaction mass; 2) change in the percentage of the high-molecular polyester in the reaction mass; 3) change in the percentage of the low-molecular polyester in the reaction mass; 4) change in the percantage of free acid in the reaction mass.

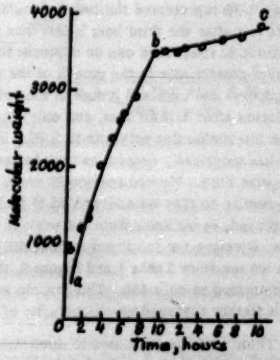

Fig. 2. ab) Change in the molecular weight as determined by viscosity when the reaction is performed at 200° in a current of nitrogen; bc) change in the molecular weight as determined by viscosity when the reaction is performed at 200° in vacuo.

During the first half-hour it is chiefly the low-molecular polyester that is produced, the total polyester constituting 67.0% by weight of the total reaction mass in the first sample, though this product contains only 9.1% of a high-molecular polyester with a molecular weight of approximately 900, i.e., the trimer. The rest of the polyester is a low-molecular product with a molecular weight below 900, i.e., consisting for the most part of a mixture of the dimer and other products (see below), constituting 90.9% of the total weight of the polyester. It is apparent that the reaction occurs as follows in this stage:

$$HO(CH_2)_6OH + HOOC(CH_2)_8COOH \rightarrow H[O(CH_2)_6OOC(CH_2)_8CO]OH + H_2O. \quad (I)$$

$$H[O(CH_2)_6OOC(CH_2)_8CO]OH + HO(CH_2)_6OH \rightarrow HO(CH_2)_6OOC(CH_2)_8COO(CH_2)_6OH. \quad (II)$$

$$HO(CH_2)_6OOC(CH_2)_8COOH + HOOC(CH_2)_8COOH \rightarrow H_2O + HOOC(CH_2)_8COO(CH_2)_6OOC(CH_2)_8COOH. \quad (III)$$

$$\left.\begin{array}{l}\text{(II)} + HOOC(CH_2)_8COOH \\ \text{(III)} + HO(CH_2)_6OH\end{array}\right\rightarrow H[O(CH_2)_6OOC(CH_2)_8CO]_2OH + H_2O.$$
(IV)

I) Acid ester of hexamethylene glycol and sebacic acid; II) di-(hexamethylene glycol) ester of sebacic acid; III) acid ester of hexamethylene glycol and sebacic acid; IV) dimer.

The other compounds formed are the products of the reaction of the dimer (IV) with hexamethylene glycol (V) and sebacic acid (VI); thus, the low-molecular polyester, which is soluble in diethyl ether, is probably a mixture of compounds (I, II, III, IV, V, and VI), the molecular weight of each of them lying below 800. The trimer

$$H[O(CH_2)_6OOC(CH_2)_8CO]_3OH$$

has a molecular weight of 868 and is no longer soluble in diethyl ether. Thus, within half an hour after the onset of the reaction, the reaction mass contains a mixture of condensed polymerization products, with two to six residues (trimer) of the glycol and the acid, together with the initial substances, which constitute 23% by weight of the total reaction mass. As the reaction proceeds, the percentage of the monomer in the reaction mass continues to fall, with the percentage of the polyester rising. Thus, within an hour and a half, the percentage of the polyester constituted 93.9% of the reaction mass by weight, 46.8% representing the high-molecular polyester, i.e., the ester insoluble in diethyl ether. After 2.5 hours had elapsed, the polyester totaled 95.6%, 82.3% of this representing the high-molecular polyester. During this period the reaction involved the further exhaustion of the initial substances (as indicated by the diminution of the percentage of the free acid in the reaction mass to 2.7%) as well as the reaction of the molecules of the low-molecular polyester with one another. This idea is based upon the fact that the rise of the molecular weight of the polyester to 1271 is paralleled by a drop in the percentage of the low-molecular polyester to 13.3%. At the same time the reaction gradually slowed down, so that by the end of the tenth hour, the polyester constituted 100%, of which only 3.9% represented the low-molecular polyester. When we bear in mind that the percentage of the initial substances left after the third hour is less than 3%, while both the percentage and the molecular weight of the polyester continue to rise, there can be no doubt that the reaction of the polyester molecules with one another begins to play an ever-greater role in the growth of the polyester chain, this being also borne out by the fact that the percentage of free hydroxyl and carboxyl groups in the polyester falls (the acid number of the polyester was 50.5 ml of a 0.02 N alkali solution after half an hour, and only 17.6 ml after 10 hours had elapsed), as well as by the drop in the percentage of the low-molecular polyester to 3.9%. By the end of the tenth hour the rise in the molecular weight of the polyester has practically ceased, as may be seen in Figure 2, which shows the change in the molecular weight of the polyester with time. We had previously come to the conclusion that further heating of the polyester would not produce any results, so that we endeavored to find out what would be the effect of heating in vacuo, a procedure that is often employed, as we know from the work of Carothers, in the production of high-molecular polyesters [22]. With this as our objective we continued to heat the polyester for another 10 hours at the same temperature in vacuo (1.5-2 mm). As we see from Table 1 and Figure 2, the results of this heating were negligible, the increase in the molecular weight amounting to only 450. This sample was then heated in the same vacuum, but at a higher temperature (260°). This immediately produced an abrupt jump of 1500 in the molecular weight (Table 1).

These findings were used to determine the reaction order and its velocity constant. Calculation of the velocity constants from the usual formulas indicated that the constants calculated for a second-order reaction had a more constant value; we therefore concluded that this was a second-order reaction, with a velocity constant of 0.16 $min.^{-1}g^{-1}$.

The reasons why chain growth ceases in a polyesterification reaction. As we see from the figures in Table 1, the rate of growth of the polyester's molecule chain drops sharply as the percentage of monomers in the reaction mass decreases. After 9 hours of heating, when all the initial products have been completely consumed, chain growth ceases almost completely, and even heating in vacuo for 10 hours at the same temperature does not produce as much of a change in the molecular weight as, say, heating in a current of nitrogen at 200° without any vacuum and with only 1.4% of sebacic acid present in the reaction mass. Whence we may conclude that the initial substances have to be present, even though their percentage be small, to activate the polyesterification process. We checked this assumption by running tests in which various amounts of the acid, the glycol, and other substances were added to the polyester, and the effect of these additions upon the growth of the polyester chain was observed. The initial substance we used was a polyester prepared from sebacic acid and hexanediol under the conditions described above. Equimolar proportions of the initial substances were used. The tests were run as follows: a weighed portion of the acid or of the glycol was added to a weighed portion of the polyester, and then the polyester was heated to 200° in a current of nitrogen for varying lengths of time. Then the molecular weight of the polyester was determined from the viscosity of its benzene solution (0.5% concentration). The results obtained are listed in Table 2.

The results tabulated in Table 3 are plotted in Figure 3. We see from the table and the graph that adding sebacic acid or hexanediol or the two of them together and heating the mixture results in raising the molecular weight of the polyester, the hexanediol being less effective than the sebacic acid, and the latter less effective than the simultaneous addition of the acid and the glycol, which yields the best results as far as increasing the molecular weight of the polyester is concerned. It is worthy of note that the percentage of glycol or acid added is also important:

TABLE 2*

Test No.	Grams of polyester	Grams of sebacic acid or glycol	% added by weight	Molar ratio of acid to glycol	Heating time, hours	Specific viscosity of a 0.5% solution	Molecular weight
1	2.0376	–	–	–	5	0.105	3577
2	3.9933	0.0599(a)	1.5	1:1	1	0.123	4196
		0.0349(g)					
					2	0.134	4565
					3	0.142	4887
					4	0.154	5247
					5	0.164	5587
					10	0.165	5621
3	0.4933	0.0074(a)	1.5	–	5	0.146	4974
4	0.8800	0.0132(g)	1.5	–	5	0.136	4633
5	0.3540	0.0177(a)	5	1:1	5	0.142	4887
		0.0103(g)					
6	0.4600	0.0023(cs)	0.5	–	5	0.205	6984
7	1.0667	0.0265(a)	2.5	1:1	5	0.142	4887
		0.0155(g)					
8	0.3867	0.0058(a)	1.5	1:1	5	0.164	5587
		0.0034(g)					

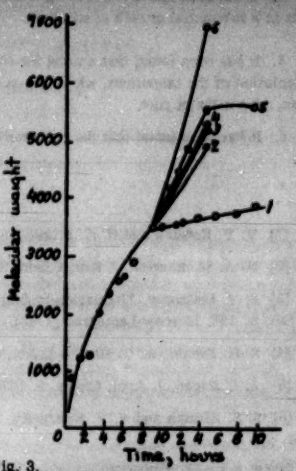

Fig. 3.
1 - Change in molecular weight of the polyester during condensed polymerization, by the viscosity method (Fig. 2); 2 - change in molecular weight when 1.5% of hexanediol is added to the polyester; 3 - change in molecular weight when 5% of the initial monomers is added to the polyester; 4 - change in molecular weight when 1.5% of sebacic acid is added to the polyester; 5 - change in molecular weight when 1.5% of the initial monomers is added; 6 - change in molecular weight when 0.5% of camphorsulfonic acid is added.

when 1.5% is added, the rise of the molecular weight is greater than when 2.5% or 5% is added. It may be that when the higher percentages are added, the added substance exhibits a destructive action. Camphorsulfonic acid was found to be even more effective; when only 0.5% was added, it nearly doubled the increase in molecular weight, that is, it did more than we achieved by heating to 260° in vacuo for 20 hours, when we succeeded in attaining a molecular weight of 6400. The action of small additions may be explained by merely assuming that these additives act catalytically, bringing about an acceleration of the reaction, which is extremely slow when they are not present. This catalytic effect is present in the glycol as well as in the acid, a stronger acid producing a greater effect even for a lesser quantity, as we have seen in the case of camphorsulfonic acid. In all our investigated cases the action of the additive diminishes with time, which may be due to the gradual depletion of the catalyst, as is observed in the process of its own polyesterification (Table 1). It may be concluded, therefore, that the intial substances, i.e., the dicarboxylic acid and the glycol, act as catalysts during the polyesterification process, which practically ceases when they are absent. Hence, the depletion of the initial monomers or of specially added catalysts must be included as another reason for the cessation of chain growth during a polyesterification reaction.

SUMMARY

1. A study has been made of the kinetics of the polyesterification of hexamethylene glycol and sebacic acid under various conditions, including the addition of acids and glycols.

2. It has been found that at the start the reaction is principally an interaction of the initial monomers with each other, yielding low-molecular polyesters; but as the process proceeds, the reaction of the polyesters molecules with one another begins to predominate, so that toward the end this process of chain growth predominates.

3. It has been found that the initial monomers act as catalysts of the polyesterification process, the reaction rate dropping as they are depleted and nearly reaching zero toward the end of the reaction because of the absence of the monomers.

*Notes to Table 2: 1) (a) denotes sebacic acid, (g) glycol, and (cs) camphorsulfonic acid; 2) The polyester used in Tests 7 and 8 was the polyester that had been heated for 10 hours in Test 2.

4. It has been found that adding small amounts of the monomers to the polyester and then heating the latter results in a substantial growth of its chain.

5. It has been found that among the reasons for a cessation of chain growth in the polyesterification reaction, the depletion of the monomers, which act as catalysts and are absolutely indispensable for the polyesterification process, play a major part.

6. It has been found that the polyesterification of glycols and dicarboxylic acids is a reaction of the second order.

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* See Consultants Bureau translation, p. 1221

THE SYNTHESIS OF SYMMETRICAL DIBROMO-, DINITRO-, AND SOME DIHYDROXYAZONAPHTHALENES

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Compounds of the Hal–R–N=N–R–Hal or (O_2N)–R–N=N–R–(NO_2) type, in which halogen atoms or nitro groups replace hydrogen atoms of benzene or naphthalene ring systems that are symmetrically arranged about the azo group, cannot be synthesized by the usual coupling method, as we know, because halogen or nitro derivatives of benzene and naphthalene do not enter into coupling reactions. The same difficulties are encountered in the syntheses of dihydroxyazo derivatives of naphthelene whenever the azo group is not located at the usual coupling position, as governed by the OH group. As a result, whenever azo compounds of the above-mentioned types have to be synthesized, the simple azo coupling method has to be abandoned and other, more complicated methods employed, often producing a very low yield of the product. It is quite likely that this is why so few azo compounds of the above-mentioned type have been described in the literature.

One of the present authors previously found [1, 2] that when the experimental conditions were modified somewhat, the well-known Sandmeyer's reaction, which enables us to procure symmetrical derivatives of aromatic hydrocarbons, can also be utilized to synthesize high yields of symmetrical azo compounds. As a first approximation, we also suggested the mechanism underlying this interesting conversion [1]. Bearing in mind that the conversion objects in our previous researches were chiefly amines of the benzene series, in our further study of the feasibility of applying the method we had discovered as well as of its mechanism and of the conditions affecting its application, we took several bromo, nitro, and hydroxy derivatives of 1- and 2- naphthylamine for our further research. If the process were successful, the latter compounds should yield the respective dibromo- dinitro-, and dihydroxyazonaphthalenes, not previously described in the literature and of some interest.

Our experiments bore out our expectations; we synthesized 1,1'-dibromo-2,2'-azo-naphthalene from 1-bromo-2-naphthylamine , 4,4'-dibromo-1,1'-azonaphthalene from4-bromo-1-naphthylamine, 5,5'-dibromo-1,1'-azonaphthalene from 5-bromo-1-naphthylamine, 5,5'-dinitro-1,1'-azonaphthalene from 5-nitro-1-naphthylamine, 4,4'-dinitro-1, 1'-azonaphthalene from 4-nitro-1-naphthylamine, 5,5'-dihydroxy-1,1'-azonaphthalene from 1,5-aminonaphthol, and 7,7'-dihydroxy-1,1'-azonaphthalene from 1,7-aminonaphthol.

The exception was the synthesis, in two cases, of dinaphthyl derivatives instead of the expected azo compound, which we have been unable, as yet, to explain on theoretical grounds though this was no surprise, as we had observed analogous instances previously [1]; 8-nitro-1-naphthylamine yielded 8,8'-dinitro-1,1'-dinaphthyl instead of the azo products, while 1-nitro-2-naphthylamine yielded 1,1'-dinitro-2,2'-dinaphthyl. The negative influence of a nitro group in the ortho position to the diazo group may also be illustrated by our failure to secure, 2,2'-dinitro-1,1'-azonaphthelene from the diazo compound 2-nitro-1-naphthylamine, the reaction product always turning out to be nothing but tar. At the same time it is worthy of note that no such difficulty was encountered in synthesizing the corresponding dinitroazonaphthalene from diazo-1-nitro-2-naphthylamine.

EXPERIMENTAL

1. Preparation of a copper catalyst solution. 28.5 grams of copper sulfate was dissolved in 100 ml of hot water, and then 30 ml of a 25% ammonia solution was added. 7 grams of hydroxylamine hydrochloride dissolved in 20 ml of water was added to the resulting dark-blue solution while it was still warm. The amount of the cuprous salt thus produced was used in each of the tests described below (per 0.1 mole of the amine).

2. Synthesis of 1,1'-dibromc 2,2'-azonaphthalene. 22.2 grams of 1-bromo-2-naphthylamine with an m.p. of 63°, prepared by the method suggested by Lallmann and Schmidt [3], was dissolved by heating it in 18 ml of 20% hydrochloric acid and 7 ml of water. The resultant pasty grey mass was chilled to 0° and then diazotized

with a solution of 7 g of sodium nitrite in 20 ml of water, after which it was diluted with ice water to make 1 liter and filtered. The diazo solution produced was added during the course of 5 minutes, with vigorous stirring, to a chilled solution of the copper catalyst (it is best to remove the film that is formed by adding small amounts of ether). After stirring had been continued for one hour, the precipitated reaction product was suction-filtered out and washed on the filter successively with water, dilute hydrochloric acid, water, dilute alkali, and again with water, after which it was dried. Double recrystallization from toluene yielded 8.8 g of the pure product, or 40% of the theoretical. Red needles with an m.p. of 252°, which are insoluble in water or alcohol, and sparingly soluble in benzene.

6.296 mg substance: 0.350 ml N_2 (22.5°, 733.5 mm) (Microanalysis by the Dumas method).
Found %: N 6.20. $C_{22}H_{12}N_2Br_2$. Calculated %: N 6.36.

3. Synthesis of 4,4'-dibromo-1,1'-azonaphthalene. 22.2 grams of 4-bromo-1-naphthylamine, prepared by the Meldola method [4], was diazotized and processed as set forth above. The yield of the unpurified product was 16.5 g or 75% of the theoretical. Double recrystallization from toluene yielded 12 g of the pure product, or 50% of the theoretical. Red needles with an m.p. of 268°, slightly soluble in alcohol and benzene, and insoluble in water.

6.812 mg substance: 0.374 ml N_2 (23.5°, 728.5 mm). Found %: N 6.07. $C_{22}H_{12}N_2Br_2$. Calculated %: N 6.36.

4. Synthesis of 5,5'-dibromo-1,1'-azonaphthalene. 22.2 grams of 5-bromo-1-naphthylamine, prepared by the Guareschi method [5], was diazotized and processed as set forth above. The yield of the crude product totalled 18 g, or 82% of the theoretical. Double recrystallization from benzene yielded 8.8 g of the purified product, or 40% of the theoretical. Dark-brown needles with an m.p. of 210°, insoluble in water or alcohol, slightly soluble in benzene.

6.886 mg substance: 0.380 ml N_2 (22°, 731.3 mm). Found %: N 6.14. $C_{22}H_{12}N_2Br_2$. Calculated %: N 6.36.

5. Synthesis of 8,8'-dinitro-1,1'-dinaphthyl. 18.8 grams of 8-nitro-1-naphthylamine, prepared by the Meldola method [6], was diazotized in a chilled, strongly acid solution (large excess of conc. sulfuric acid). The resultant diazo solution was quickly poured into ice water, filtered, and neutralized with ammonia until its reaction was weakly acid, after which it was used for reactions with the copper catalyst solution under the conditions described above. The yield of the crude product was 16.8 g, or 86% of the theoretical. Double recrystallization from toluene yielded 8.1 g of the pure product, or 43.5% of the theoretical. A finely crystalline yellow powder with an m.p. of 275° insoluble in water or alcohol.

4.671 mg substance: 0.487 ml N_2 (26.5°, 727 mm). Found %: N 8.09. $C_{22}H_{12}O_4N_2$. Calculated %: N 8.12.

6. Synthesis of 5,5'-dinitro-1,1'-azonaphthalene. 18.8 grams of 5-nitro-1-naphthylamine, prepared by the Meldola method [6], was diazotized and processed under the conditions set forth above. The yield of the crude product totaled 12.4 g, or 63% of the theoretical. Double recrystallization from toluene yielded 2.5 g of the pure substance, or about 14% of the theoretical. A yellow crystalline powder with an m.p. of 280°, insoluble in water or alcohol, and soluble in hot benzene and toluene.

3.786 mg substance: 0.513 ml N_2 (23.5°, 728 mm). Found %: N 14.96. $C_{22}H_{12}O_4N_2$. Calculated %: N 15.05.

7. Synthesis of 1,1'-dinitro-2,2'-dinaphthyl. 18.8 grams of 1-nitro-2-naphthylamine was diazotized under the conditions described by Vesely [7] (passing N_2O_3 through a solution of nitronaphthylamine in hydrochloric acid chilled to 0°, and then removing the excess of nitrous acid with urea). The resultant diazo solution was then diluted with ice water to make 1 liter and poured into the copper catalyst solution, the further processing being the usual one set forth above. The yield of the crude product totaled 8.4 g or 43% of the theoretical. Double recrystallization from toluene yielded 2 g of the pure substance, or about 11.5% of the theoretical. Yellow needles with an m.p. of 264-270°, insoluble in water, alcohol, or acetone, and slightly soluble in benzene.

3.698 mg substance: 0.284 ml N_2 (23.5°, 728 mm). Found %: N 8.47. $C_{22}H_{12}O_4N_2$. Calculated %: N 8.12.

8. Synthesis of 4,4'-dinitro-1,1'-azonaphthalene. 18.8 grams of 4-nitro-1-naphthylamine, prepared by nitrating and then saponifying 1-acetonaphthylamine [8], was diazotized and processed under the conditions set forth above. The yield of the crude product was 14 g, or about 72% of the theoretical. Double recrystallization from toluene yielded 2 g of the pure product, or about 11.5% of the theoretical. A yellow crystalline powder with an m.p. of 310°, insoluble in water or alcohol, and slightly soluble in benzene and toluene.

4.297 mg substance: 0.596 ml N_2 (25.5°, 727 mm). Found %: N 15.16. $C_{22}H_{12}O_4N_2$. Calculated %: N 15.05.

9. Synthesis of 5,5'-dihydroxy-1,1'azonaphthalene. 19.4 grams of 1,5-aminonaphthol hydrochloride was dissolved in 25 ml of conc. hydrochloride acid and 50 ml of water. The solution was then chilled to 2 to 3° and diazotized with a solution of 7 g of sodium nitrite in 20 ml of water (the process is rapid, and is accompanied by considerable foaming). The diazo solution was then diluted with ice water to make 1 liter, filtered, and processed as described above. Double recrystallization from pyridine yielded 2.85 g of the pure azo compound, or 54% of the theoretical. A dark-blue powder with an m.p. of 360°. It dissolves in alkalies, coloring them dark red, is sparingly soluble in alcohol and in toluene and freely soluble in pyridine.

4.817 mg substance: 0.390 ml N_2 (26.5°, 732 mm). Found %: N 8.96. $C_{20}H_{14}O_2N_2$. Calculated %: N 8.91.

10. Synthesis of 7,7'-dihydroxy-1,1'-azonaphthalene. 19.4 grams of aminonaphthol hydrochloride was diazotized and processed under the conditions specified for the previous case. Recrystallization from alcohol, followed by another recrystallization from acetone, yielded 13.5 g of the azo product, or 86% of the theoretical.

A black powder with an m.p. above 360°. It dissolves in alkalies, coloring them red, and is sparingly soluble in alcohol, benzene, acetone, and pyridine.

4.647 mg substance: 0.367 ml N_2 (25.5°, 733 mm). Found %: N 8.71. $C_{20}H_{14}O_2N_2$. Calculated %: N 8.91.

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THE N-ARYL AMIDES OF HYDROXY CARBOXYLIC ACIDS AND THEIR CONVERSION INTO HETEROCYCLIC COMPOUNDS

XVII. THE INTRAMOLECULAR CONDENSATION OF ARYL AMIDES OF β,β-DIPHENYL-β-HYDROXYPROPIONIC ACID

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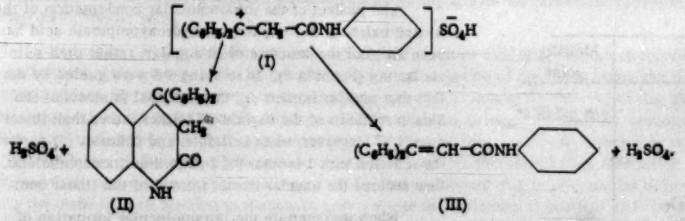
The aryl amides of β,β-diphenyl-β-hydroxypropionic acid form halochromic salts with concentrated sulfuric acid. Inasmuch as these salts are looked upon as active coordination compounds [1], in which intramolecular condensation may occur, we were interested in the feasibility of converting the aryl amides of β,β-diphenyl-β-hydroxypropionic acid into the respective heterocyclic compounds.

The possible intramolecular conversions within the cation of the halochromic salt of β,β-diphenyl-β-hydroxypropionanilide may be represented as follows:



Coordination of the carbonium carbon atom with the ortho carbon atom of the phenyl radical attached to the nitrogen results in the formation of 4,4-diphenylhydrocarbostyril (II). On the other hand, the carbonium carbon atom can be coordinated with the carbon of the methylene group, which would then have to yield β,β-diphenylacrylanilide (III). Hence, the carbonium ion of the halochromic salt of an aryl amide of β,β-diphenyl-β-hydroxypropionic acid has two nucleophilic centers, the carbonium carbon atom being able to coordinate with one center or the other, depending upon the reaction conditions.

Experiments have fully confirmed our conjecture. When we reacted β,β-diphenyl-β-hydroxypropionanilide with concentrated sulfuric acid, we secured two substances: one with an m.p. of 131°, and another with an m.p. of 242.2-243.5°. The first one satisfied the figures given in the literature for β,β-diphenylacrylanilide [2]. When we oxidized it with potassium permanganate in an alkaline medium, we secured benzophenone, which established that the structure of the substance with an m.p. of 131° was that of β,β-diphenylacrylanilide (III).

The second substance is not affected by a slightly alkaline solution of potassium permanganate and has a high melting point, which is typical of the type of heterocyclic compounds we have been studying. These facts, as well as the findings of a complete analysis, enable us to assign the second possible structure to the substance with an m.p. of 242.5-243.5°, namely, 4,4-diphenylhydrocarbostyril (II), in conformity with the theory of chemical structure.

In order to extend the methods of synthesizing the aryl amides of β,β-diphenylacrylic acid, we ran tests with $(C_6H_5)_2C(OH)CH_2CONHAr$ where Ar = p-$C_6H_4CH_3$, o-$C_6H_4CH_3$, p-$C_6H_4OCH_3$ and p-$C_6H_4OC_2H_5$. The reaction

was simple, no more than 10 minutes being required for completion of the experiment, and the product being secured in the individual state with a yield of 75-85%. The properties of the synthesized aryl amides of β,β-diphenylacrylic acid are listed in Table 1.

TABLE 1

No.	Aryl amide formula	Melting point	Melting point given in the literature
1	$(C_6H_5)_2C{=}CHCONHC_6H_5$	131°	130 - 131° [2]
2	$(C_6H_5)_2C{=}CHCONHC_6H_4CH_3$-p	158.5	
3	$(C_6H_5)_2C{=}CHCONHC_6H_4CH_3$-o	141	
4	$(C_6H_5)_2C{=}CHCONHC_6H_4OC_2H_5$-p	157	
5	$(C_6H_5)_2C{=}CHCONHC_6H_4OCH_3$-p	165	163° [3]

The aryl amides of β,β-diphenylacrylic acid may be synthesized, with less satisfactory results, in the presence of anhydrous zinc chloride. The reaction then requires a longer time at higher temperature, and the yield of the reaction product is lower.

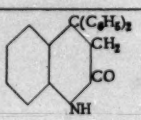
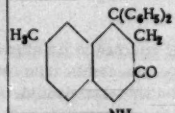
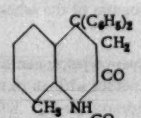
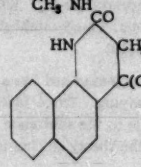
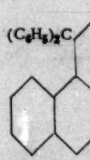
Research during the past few years has established the presence of an anesthetic effect of esters of β,β-diphenylacrylic acid [4]. In this connection, the development of ways of synthesizing aryl amides of β,β-diphenylacrylic acid and a study of their properties are of indisputable interest in identifying this class of anesthetics.

Aryl amides of β,β-diphenyl-β-hydroxypropionic acid

$$(C_6H_5)_2C(OH)CH_2CONHAr,$$

where Ar = p-$C_6H_4CH_3$, o-$C_6H_4CH_3$, α-$C_{10}H_7$ and β-$C_{10}H_7$, were used in synthesizing derivatives of 4,4-diphenylhydrocarbostyril. The properties of the synthesized compounds are givein in Table 2.

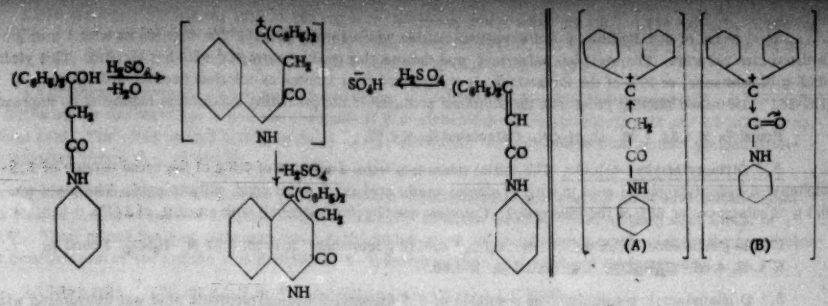
TABLE 2

No.	Formula	Melting point
1		242.5-243.5°
2		289
3		198.5
4		280
5		285

The product of the intramolecular condensation of the β-naphthalide of β,β-diphenyl-β-hydroxypropionic acid has been assigned the structure of an angular, rather than a linear isomer (Formula 5). In so doing we were guided by the fact that angular isomers are the principal products of the Skraup synthesis of the naphthoquinolines rather than linear ones [5]. Moreover, when Lellmann and Schmidt [6] performed the reaction with 1-bromo- and 1-nitro-2-aminonaphthalene, they secured the angular isomer instead of the linear one.

When we compare the intramolecular formation of an ethylenic bond with the closure of a heterocyclic ring in the aryl amides of β,β-diphenyl-β-hydroxypropionic acid, we note that the former takes place much more easily than the latter. Formation of an aryl amide of β,β-diphenylacrylic acid requires less heating time, and anhydrous zinc chloride may be utilized as the dehydrating agent, though anhydrous zinc chloride proved to be utterly useless for intramolecular ring closure.

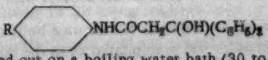
Inasmuch as the aryl amides of β,β-diphenylacrylic acid we synthesized form colored halochromic salts with conc. sulfuric acid, we were interested in the feasibility of converting them into derivatives of tetrahydroquinoline. To do that, we dissolved aryl amides of β,β-diphenylacrylic acid in conc. sulfuric acid, heating the resulting yellow solution until it turned emerald green. This yielded a compound that was the same as the product of the condensation of the aryl amides of β,β-diphenyl-β-hydroxypropionic acid. The foregoing may be illustrated by the following diagram:



The reaction was carried out with $(C_6H_5)_2C{=}CHCONHAr$, where Ar = C_6H_5, p-$C_6H_4CH_3$ and o-$C_6H_4CH_3$. Using these examples, we established that aryl amides of β,β-diphenylacrylic acid could be converted into derivatives of 4,4-diphenylhydrocarbostyril by the action of conc. sulfuric acid.

The aryl amides of β,β-diphenyl-β-hydroxypropionic acid are condensed more slowly than aryl amides of benzilic acid. Closure of the heterocyclic ring usually requires several minutes of heating on a water bath (80-90°), whereas in aryl amides of benzilic acid the five-membered ring is closed within 30 seconds at 50° [7]. Intramolecular ring closure in the cation of a halochromic salt is an electronophilic reaction, the difference in the ease of ring closure between the aryl amides of β,β-diphenyl-β-hydroxypropionic acid and those of benzilic acid being attributable to the differences between the electronophilic activity of the carbonium carbon atoms in the cations of their halochromic salts.

In the cation (A) the repulsion of electrons by the CH_2 group diminishes the electronophilic activity of the carbonium carbon atom, while in the cation (B), the polarization of the C=O group and the attraction of electrons adds to the positive charge on the carbon atom and accelerates the velocity of ring closure. Furthermore, there can be no doubt that the differences in the distances between the reaction centers also make themselves felt in closure of the six- and five-membered rings. Another, no less significant, fact is that substituents attached to the nitrogen atom of the radical affect the closure of six- and five-membered rings differently. Such substituents as Alk or OAlk either do not affect the closure of the five-membered ring in aryl amides of benzilic acid when they are in the ortho or para position to the amide group or else this influence is so slight as to be practically negligible [8]. Another state of affairs is seen in the condensation of the aryl amides of β,β-diphenyl-β-hydroxypropionic acid when strong Class I orienting groups are present in their radicals attached to the nitrogen atom at the para position to the aryl amide group. We ran our experiments with



where R = OCH_3 and OC_2H_5. The reaction was carried out on a boiling water bath (30 to 40 minutes). This yielded the p-aniside and the p-phenetide of β,β-diphenylacrylic acid, no ring closure taking place. Considerable tarring occurred when a higher temperature was used or heating was continued for a longer time.

We know that Class I orienting groups have been found to oppose cyclization in the synthesis of quinoline derivatives. Marckwald and Schmidt [9], for example, found that acetylacetone does not yield aminoquinoline when reacted with p-phenylenediamine in a Dobner-Miller reaction. Roberts and Turner [10] used a series of examples to show that strong Class I orienting groups prevent the formation of quinoline derivatives when they are in the para position to the nitrogen atom.

EXPERIMENTAL

β,β-Diphenylacrylanilide. a) 5 ml of conc. sulfuric acid was added to a solution of 1 g of β,β-diphenyl-β-hydroxypropionanilide in 5 ml of glacial acetic acid. The reaction mass was heated on a water bath (80-90°) for 10 minutes, the color of the mass changing from yellow to ruby-red. The contents of the flask were then poured out into water, the reaction product being recovered in the usual manner. This yielded 0.7 g of substance, or 74% of the theoretical. The anilide was insoluble in water, but dissolved when heated in the usual organic solvents. It crystallized from alcohol as colorless needles with an m.p. of 131°. When it was oxidized with potassium permanganate in an alkaline medium, we obtained a substance with an m.p. of 47°, which agrees with the figure given in the literature for benzophenone [11]. The m.p. of β,β-diphenylacrylanilide is given as 131° in the literature [2].

b) 1 Gram of β,β-diphenyl-β-hydroxypropionanilide was heated to 180-190° for 45 minutes with 1 g of anhydrous zinc chloride. The melt was pulverized, and the reaction product extracted with hot alcohol. This yielded 0.35 g of substance, or 36% of the theoretical. It crystallized from alcohol as colorless needles with an m.p. of 130-131°. Its mixed melting point with the substance produced in the preceding experiment exhibited no depression.

Found %: N 4.84, 4.96. $C_{21}H_{17}ON$. Calculated %: N 4.67.

β,β-Diphenylacrylo-o-toluide. The initial substances were: a solution of 0.5 g of the ortho toluide of β,β-diphenyl-β-hydroxypropionic acid in 5 ml of glacial acetic acid and 2 ml of conc. sulfuric acid. The yield was 0.4 g of substance, or 85% of the theoretical. Colorless needles (from alcohol) with an m.p. of 141°.

0.0125 g substance: 3.95 ml 0.01 N H_2SO_4. 0.0112 g substance: 3.75 ml 0.01 N H_2SO_4. Found %: N 4.42, 4.68. $C_{22}H_{19}ON$. Calculated %: N 4.46.

β,β-Diphenylacrylo-p-toluide. The p-toluide of β,β-diphenyl-β-hydroxypropionic acid was dehydrated with conc. sulfuric acid, the yield being 83% of the theoretical. Colorless needles (from alcohol) with an m.p. of 158.5°. Oxidation of the β,β-diphenylacrylo-p-toluide with potassium permanganate in an alkaline medium yielded benzophenone (m.p. 47°) [11].

0.0166 g substance: 5.43 ml 0.01 N H_2SO_4. 0.0172 g substance: 5.72 ml 0.01 N H_2SO_4. Found %: N 4.58, 4.6. $C_{22}H_{19}ON$. Calculated %: N 4.46.

β,β-Diphenylacrylo-p-aniside. Initial substances: a solution of 0.8 g of the para aniside of β,β-diphenyl-β-hydroxypropionic acid in 4 ml of glacial acetic acid and 5 ml of conc. sulfuric acid. This yielded 0.61 g, or 84% of the theoretical. Crystallization from alcohol yielded minute needles with an m.p. of 165°. The m.p. of β,β-diphenylacrylo-p-aniside is given as 163° in the literature [3].

Found %: N 4.08, 4.04. $C_{22}H_{19}O_2N$. Calculated %: N 4.25.

β,β-Diphenylacrylo-p-phenetide. This was synthesized by heating a solution of the para phenetide of β,β-diphenyl-β-hydroxypropionic acid with conc. sulfuric acid. The yield totaled 75% of the theoretical. Colorless needles (from alcohol) with an m.p. of 157°.

0.0134 g substance: 3.9 ml 0.01 N H_2SO_4. 0.0105 g substance: 3 ml 0.01 N H_2SO_4. Found %: N 4.07, 4. $C_{23}H_{21}O_2N$. Calculated %: N 4.08.

4,4-Diphenyl-2-oxotetrahydroquinoline. (4,4-Diphenylhydrocarbostyril). a) 0.5 g of β,β-diphenyl-β-hydroxypropionanilide was heated on a water bath (80-90°) with 2.5 ml of conc. sulfuric acid until all the anilide had dissolved and the mixture's bright-yellow color had turned emerald-green. After the reaction mass had cooled it was poured into five times its weight of water. The resulting precipitate was processed in the usual manner, yielding 0.47 g or 95% of the theoretical. The substance was insoluble in water, though freely soluble in acetone and chloroform. It crystallized from alcohol as colorless needles with a m.p. of 242.5-243.5°.

b) 0.5 g of β,β-diphenylacryloanilide was heated on a boiling water bath with 2.5 ml of conc.sulfuric acid for 20-25 minutes. The reaction product was precipitated as in the preceding experiment yielding 0.4 g of the substance, or 80% of the theoretical. Colorless needles (from alcohol) with a m.p. of 242.5-243.5°. Its mixed melting point with the 4,4-diphenylhydrocarbostyril synthesized in the first test exhibited no depression.

0.1042 g subs.: 0.3211 g CO_2; 0.0539 g H_2O. 0.1032 g subs.: 0.3182 g CO_2; 0.0516 g H_2O. 0.2630 g subs.: 8.54 ml 0.1 N H_2SO_4. 0.1840 g subs.: 6 ml 0.1 N H_2SO_4. 0.0117 g subs.: 0.0959 g camphor: Δt 16.2°. Found %: C 84.1, 84.14; H 5.79, 5.55; N 4.54, 4.66; M 301. $C_{21}H_{17}ON$. Calculated %: C 84.28; H 5.69; N 4.67; M 299.

4,4-Diphenyl-2-oxo-6-methyltetrahydroquinoline. (4,4-Diphenyl-6-methylhydrocarbostyril). a) Initial substances: 1 g of the p-toluide of β,β-diphenyl-β-hydroxypropionic acid and 4.5 ml of conc.sulfuric acid. This yielded 0.9 g of substance, or 94% of the theoretical. Crystallization from glacial acetic acid yielded tetrahedral prisms with a m.p. of 289°.

b) We used the following for the reaction: 0.3 g of the p-toluide of β,β-diphenylacrylic acid and 1.5 ml of conc.sulfuric acid. The yield was 0.2 g, or 66% of the theoretical. Colorless prisms (from glacial acetic acid) with a m.p. of 289°. Their mixed melting point with the 4,4-diphenyl-6-methylhydrocarbostyril synthesized in the preceding test exhibited no depression.

3.245 mg subs.: 10.043 mg CO_2; 1.890 mg H_2O. 3.010 mg subs.: 9.340 mg CO_2; 1.650 mg H_2O. 7.140 mg subs.: 0.303 ml N_2 (24°, 743 mm). 6.070 mg subs.: 0.262 ml N_2 (24°, 743 mm). Found%: C 84.38, 84.60; H 6.51, 6.13; N 4.67, 4.73. $C_{22}H_{19}ON$. Calculated%: C 84.34; H 6.07; N 4.47.

4,4-Diphenyl-2-oxo-8-methyltetrahydroquinoline. (4,4-Diphenyl-8-methylhydrocarbostyril). a) We used the following for the reaction: 1 g of the o-toluide of β,β-diphenyl-β-hydroxypropionic acid and 4.5 ml of conc. sulfuric acid. The yield totaled 0.93 g, or 94.5% of the theoretical. Crystallization from alcohol yielded colorless lamellae with a m.p. of 198.5°.

b) Initial substances: 0.5 g of the o-toluide of β,β-diphenylacrylic acid and 2.5 ml of conc.sulfuric acid. This yielded 0.42 g of substance, or 84% of the theoretical. Colorless lamellae (from alcohol) with a m.p. of 198.5°. Their mixed melting point with the 4,4-diphenyl-8-methylhydrocarbostyril synthesized by the intramolecular condensation of the anilide of β,β-diphenyl-β-hydroxypropionic acid exhibited no depression.

0.1742 g subs.: 5.62 ml 0.1 N H_2SO_4. 0.1100 g subs.: 3.5 ml 0.1 N H_2SO_4.
Found%: N 4.51, N 4.45. $C_{22}H_{19}ON$. Calculated%: N 4.46.

4,4-Diphenyl-2-oxo-7,8-benzotetrahydroquinoline. (4,4-Diphenyl-α-naphthohydrocarbostyril). Initial substances: 1 g of the α-naphthalide of β,β-diphenyl-β-hydroxypropionic acid and 5 ml of conc. sulfuric acid. The yield was 95% of the theoretical. It crystallized from alcohol as colorless rhombi with a m.p. of 280°.

0.2200 g subs.: 6.75 ml 0.1 N H_2SO_4. 0.2120 g subs.: 6.2 ml 0.1 N H_2SO_4.
Found%: N 4.29, 4.1. $C_{26}H_{19}ON$. Calculated%: N 4.01.

4,4-Diphenyl-2-oxo-5,6-benzotetrahydroquinoline. (4,4-Diphenyl-β-naphthohydrocarbostyril). This was synthesized by condensing the β-naphthalide of β,β-diphenyl-β-hydroxypropionic acid intramolecularly, using conc.sulfuric acid. The yield was 90% of the theoretical. Colorless elongated needles (from CCl_4) m.p. 285°.
0.1500 g substance: 4.4 ml 0.1 N H_2SO_4. 0.1702 g substance: 5 ml 0.1 N H_2SO_4. Found %: N 4.10, 4.11. $C_{26}H_{19}ON$. Calc.%: N 4.01.

SUMMARY

1. It has been found that there are two nucleophilic centers in the carbonium ion of a halochromic salt of aryl amides of β,β-diphenyl-β-hydroxypropionic acid, the carbonium carbon atom being able to coordinate with one center or the other, depending upon the reaction conditions, giving rise to aryl amides of β,β-diphenylacrylic acid or 4,4-diphenylhydrocarbostyril and its derivatives. Anhydrous zinc chloride, as well as conc.sulfuric acid, may be employed in synthesizing the aryl amides of β,β-diphenylacrylic acid.

2. It has been shown that the dehydration of the aryl amides of β,β-diphenyl-β-hydroxypropionic acid may be successfully utilized as a preparative method of securing aryl amides of β,β-diphenylacrylic acid. Several compounds not described previously in the literature have been synthesized.

3. The intramolecular condensation of aryl amides of β,β-diphenyl-β-hydroxypropionic acid and of β,β-diphenylacrylic acid has been employed in developing a method of synthesizing 4,4-diphenylhydrocarbostyril and its derivatives. Several compounds not described previously in the literature have been synthesized.

4. The aryl amides of β,β-diphenyl-β-hydroxypropionic acid are condensed less rapidly than the aryl amides of benzilic acid, which is attributable to the differing electrophilic power of the carbonium carbon atoms of the cations of their halochromic salts.

5. It has been found that when the aryl amides of β,β-diphenyl-β-hydroxypropionic acid contain Class I orienting groups in the p-position to the radical attached to the nitrogen atom, the reaction is confined to dehydration, no condensation taking place.

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SYNTHESIS OF ESTERS OF PHOSPHINIC ACIDS THAT CONTAIN HETEROCYCLIC RADICALS

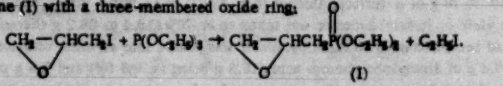
II. ETHYL ESTERS OF PHOSPHINIC ACIDS WITH HETEROCYCLIC RADICALS THAT CONTAIN OXYGEN

B.A.Arbuzov and B.P.Lugovkin

In our preceding report [1] we cited data on the synthesis of esters of phosphinic acids that contained thiazole radicals. In the present report we set forth the details of the syntheses we have effected of ethyl esters of phosphinic acids that contain radicals with one or two oxygen atoms. No such compounds have been previously investigated in the literature, nor are there any data to be found on them.

We were able to synthesize several ethyl esters of phosphinic acids that contained oxygen heterocyclic rings, by utilizing the A.E.Arbuzov reaction, in which halogen derivatives are reacted with trialkyl phosphites, or the reaction in which halogen derivatives are reacted with diethylphosphorous acid.

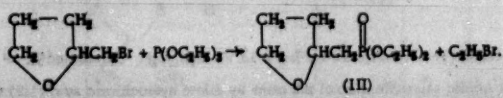
The action of triethyl phosphite upon α-epiiodohydrin, for example, yielded the ethyl esther of α-phosphono-β, γ-epoxypropane (I) with a three-membered oxide ring:



(I)

Reacting sodium diethylphosphite with α-bromomethylfuran yielded the diethyl ester of α-furfurylphosphinic acid (II).

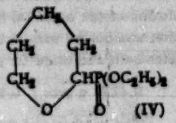
Analogously – by reacting sodium diethylphosphite or triethyl phosphite with α-bromomethyltetrahydrofuran – we synthesized the ethyl ester of α-tetrahydrofurfurylphosphinic acid (III):



(III)

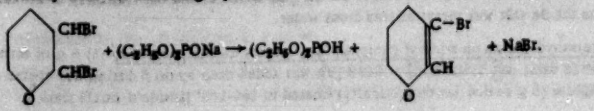
Saponifying the esters of α-furfurylphosphinic and α-tetrahydrofurfurylphosphinic acids with hydrochloric acid results in tarring of the product. Saponification with an alkali yielded the respective phosphinic acids as noncrystallizing syrups, which were analyzed as their barium salts.

The action of sodium diethylphosphite upon α-bromomethyltetrahydropyran produced satisfactory yields of the ethyl ester of α-phosphonotetrahydropyran (IV).



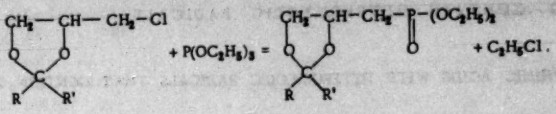
(IV)

Attempts to secure esters of phosphinic acids from α,β-dibromomethyltetrahydropyran by reacting it with sodium diethylphosphite met with failure. When the reaction was carried out in anhydrous ether, the sodium diethylphosphite split off hydrogen bromide, which reacted with the sodium diethylphosphite to yield β-bromodihydropyran in conformity with the following equations:



Nor was any success obtained in attempts to exchange the bromine atom in the β-bromodihydropyran for a diethylphosphono radical by the action of triethyl phosphite. No reaction took place even when the mixture was heated to 160°, both of the reagents being recovered unchanged.

With a view to securing phosphinic acids with heterocyclic radicals that contained two oxygen atoms we made a study of the action of triethyl phosphite upon derivatives of 4-chloromethyldioxolan-1,3. The reaction took place as follows:



The reactions resulted in the synthesis of the following phosphinic acids: 4-phosphonomethyldioxolan-1,3 (V) (R = H; R' = H); 4-phosphonomethyl-2,2-dimethyldioxolan-1,3 (VI) (R = CH_3; R' = CH_3); 4-phosphonomethyl-2-phenyldioxolan-1,3 (VII) (R = H; R' = C_6H_5); and 4-phosphonomethyl-2-p-anisyldioxolan-1,3 (VIII) (R = H; R' = $C_6H_4OCH_3$).

It is worthy of note that we were unable to secure an ester of 4-phosphonomethyldioxolan-1,3 by reacting 4-chloromethyldioxolan-1,3 with sodium diethylphosphite.

Alkaline saponification of esters of γ-4-phosphonomethyldioxolans resulted in cleavage of the dioxolan ring, yielding β,γ-dihydroxypropylphosphinic acid, in addition to the respective aldehyde or ketone.

The constants of the synthesized esters of phosphinic acids are given in the table.

EXPERIMENTAL

Action of α-bromomethylfuran on sodium diethylphosphite. 16 g of phosphorus tribromide in 25 ml of anhydrous ether was added at 25-30° to 16 g of α-furfuryl alcohol (b.p. 69-71° at 11 mm; n_D^{20} 1.4850) dissolved in 100 ml of anhydrous ether. The yield of furfuryl bromide was taken to be 70% (18.4 g; 26.2 g theoretically) [2]. After the synthesized bromide had been treated with fused potash, it was poured into an ether solution of sodium diethylphosphite, prepared from 17.4 g of diethylphosphorous acid (15.8 g being called for) and 2.6 g of metallic sodium in 150 ml of anhydrous ether during 45 minutes. The precipitated sodium bromide was filtered out and washed with ether. The ether was driven off and the residue was distilled in vacuo.

The ethyl ester of α-furfurylphosphinic acid distilled at 115-120° and 2 mm as a colorless liquid that was freely soluble in water; n_D^{20} 1.4665, yield 14.1 g (56.5% of the theoretical). After redistillation the ester had a b.p. of 117-120° at 2 mm.

n_D^{20} 1.4670; d_{20}^{20} 1.1473.

0.0956 g subs.: 25.25 ml NaOH (T = 0.0191). Found %: P 13.97. $C_9H_{13}O_4P$. Calculated %: P 14.22.

Hydrolysis of the ester. 1) Acidic saponification of the ester by dilute hydrochloric acid (1:2) in a sealed tube at 100-110° for 6 hours yielded a tarry product.

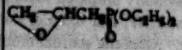
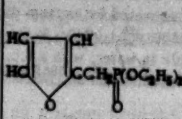
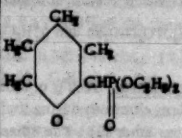
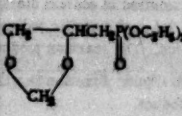
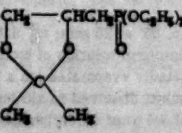
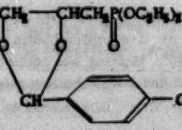
2) 1.5 g of the substance was boiled for 4 hours with 1 g of sodium hydroxide in 50 ml of water. After the solution had been evaporated to small volume, it was neutralized with hydrochloric acid (methyl orange) and then evaporated to dryness. The residue was processed by boiling it a few times with absolute alcohol. This yielded 1 g of α-furfurylphosphinic acid as a thick noncrystallizing liquid. The acid was analyzed as its Ba salt. An aqueous solution of the acid was boiled for 10-15 minutes with an excess of barium carbonate. The next day the filtered solution was boiled with activated charcoal. The Ba salt was analyzed after the solution had been evaporated on a water bath and dried for a few hours at 125-135° to constant weight.

0.4176 g subs.: 0.2006 g $BaSO_4$. Found %: Ba 28.26. $(C_4H_3OCH_2PO_2OH)_2Ba$. Calculated %: Ba 29.91.

The synthesis of the phosphinic acids and the production of the Ba salts were carried out similarly in all the ensuing tests. In some of the tests the Ba salt was recrystallized from water.

Action of α-bromomethyltetrahydrofuran on triethyl phosphite and sodium diethylphosphite. 1) 8 g of tetrahydrofurfuryl bromide (b.p. 57° at 12 mm; n_D^{20} 1.4823; d_{20}^{20} 1.3988 [3]) was added drop by drop during the course of 30 minutes to 9 g of triethyl phosphite (8 g called for theoretically) heated to 150-160° (inside a small flask[1]).

[1] The temperature was measured within the reaction mixture in every experiment.

No.	Name of the ethyl ester	Formula	B.p.	n_D^{20}	d_4^{20}
I	α-Phosphono-β,γ-epoxypropane.....		131-133° at 13 mm	1.4405	1.1373
II	α-Furfurylphosphinic acid.....		117-120 at 2 mm	1.4670	1.1473
III	α-Tetrahydrofurfurylphosphinic acid....		118-112 at 2 mm	1.4482	1.1611
IV	α-Tetrahydropyranphosphinic acid.....		123-125 at 3 mm	1.4535	1.1085
V	4-Phosphonomethyldioxolan-1,3.....		120-121 at 2.5mm	1.4440	1.1716
VI	4-Phosphonomethyl-2,2-dimethyldioxolan-1,3.....		117-119 at 4 mm	1.4380	1.1029
VII	4-Phosphonomethyl-2-phenyldioxolan-1,3.....		184-186 at 3 mm	1.4498	1.1737
VIII	4-Phosphonomethyl-2-anisyldioxolan-1,3		229-231 at 5 mm	1.5065	1.1935

Heating was continued for 1 hour at 160-165°, after which the reaction product was distilled in vacuo. The ethyl ester of α-tetrahydrofurfurylphosphinic acid distilled at 108-111° at 2 mm as a colorless liquid that was readily soluble in water. The Beilstein reaction was weakly positive. It weighed 3.6 g (33.4% of the theoretical).

n_D^{20} 1.4492; d_4^{20} 1.1075.

0.0756 g subs.: 19.22 ml NaOH (T = 0.0193). Found %: P 13.58. $C_6H_{13}O_4P$. Calculated %: P 13.96.

2) 9 g of tetrahydrofurfuryl bromide was added to an ether solution of sodium diethylphosphite prepared from 10.5 g of diethylphosphorous acid (7.5 g being called for) and 1.3 g of metallic sodium in 150 ml of anhydrous ether. A small quantity of sodium bromide settled out when the ether was boiled for 1.5 hours. 100 ml of anhydrous benzene was added, and all the ether was driven off. The benzene solution was boiled for 3 hours. The reaction product was processed appropriately and then distilled in vacuo.

The ethyl ester of α-tetrahydrofurfurylphosphinic acid had a b.p. of 110-112° at 2 mm after having been distilled twice. The yield was 3.6 g (29% of the theoretical).

n_D^{20} 1.4482; d_4^{20} 1.1011.

Found %: P 13.83. Calculated %: P 13.96.

Hydrolysis of the ester. 1.5 g of the substance was heated to boiling for 4 hours with 1.5 g of NaOH in 50 ml of water. This yielded 1.2 g of α-tetrahydrofurfurylphosphinic acid as a thick noncrystallizing liquid. Its barium salt was analyzed.

0.4132 g subs.: 0.2658 g $BaSO_4$. Found %: Ba 29.31. $(C_5H_9OCH_2PO_2OH)_2$ Ba. Calc %: Ba 29.39.

Action of α-bromotetrahydropyran on diethylphosphorous acid. Dry hydrogen bromide was passed through 14.6 g of dihydropyran (b.p. 84-86° [4]) at a temperature between 0° and +3° for 2.5 hours. The dissolved hydrogen bromide was quickly evacuated in vacuo. The synthesized bromide [5] was a reddish-brown liquid that gave off hydrogen bromide [n_D^{20} 1.5050; it weighed 26 g (28.7 g being called for)], was immediately dissolved in anhydrous ether (50 ml) and poured during the course of 10 minutes into previously prepared sodium diethylphosphite (25.5 g of diethylphosphorous acid, instead of the 21.7 g called for theoretically, and 3.6 g of metallic sodium in 200 ml of anhydrous ether). As the ether boiled up, the mixture was cooled. After the sodium bromide had been filtered out and the ether had been driven off, the following substances were recovered by vacuum distillation: 1) 6.8 g of diethylphosphorous acid, b.p. 182-185° at ordinary pressure; n_D^{20} 1.4090; d_{20}^{20} 1.0743. 2) the ethyl ester of α-tetrahydropyranphosphinic acid as an oily liquid that was readily soluble in water, with a b.p. of 130-132° at 6 mm; n_D^{20} 1.4522. It weighed 16.1 g (46% of the theoretical). The ester was redistilled at 123-125° and 3 mm.

n_D^{20} 1.4535; d_{20}^{20} 1.1085.

0.0646 g subs.: 17.32 ml NaOH (T = 0.0191). Found %: P 14.18. $C_9H_{19}O_4P$. Calculated %: P 13.96.

Hydrolysis of the ester. 3.3 g of the substance was heated to 100-105° in a sealed tube for 6 hours with 30 ml of dilute hydrochloric acid (1:2). Repeated evaporation (on a water bath) until all the HCl was eliminated yielded 2.6 g of a syrupy product. During hydrolysis of the ester by hydrochloric acid pentadiol-5,6-phosphinic acid may also be produced as the result of the rupture of the pyran ring, in addition to the α-tetrahydropyranphosphinic acid. Analysis of the Ba salt indicated that the product of saponification was pentadiol-5,6-phosphinic acid.

0.5786 g subs.: 0.2713 g $BaSO_4$. Found %: Ba 27.59. $(C_5H_9OPO_2OH)_2Ba$ and $[C_5H_9OH(CH_2)_3CHOHPO_2OH]_2Ba$. Calculated %: Ba 29.39 and 27.29.

Action of α,β-dibromotetrahydropyran on sodium diethylphosphite. 15.2 g of bromine (18 g being called for) was added drop by drop with constant chilling (snow and sodium chloride) during the course of 45 minutes to 9.5 g of dihydropyran (b.p. 84-86°), dissolved in 25 ml of anhydrous ether [6]. The ether solution of the bromide was added during the course of 20 minutes to 1 mole of an ether solution of sodium diethylphosphite 16.5 g of diethylphosphorous acid (13.1 g being called for theoretically) and 2.6 g of metallic sodium (2.18 g being called for theoretically) in 200 ml of anhydrous ether]. NaBr was precipitated. The reaction product was distilled in vacuo.

Fraction I: 50-93° at 14 mm. 13.2 g of a faintly yellowish liquid. Fraction II: 112-116° at 5 mm. 3.8 g of a colorless liquid. The residue (4.3 g) was an amorphous solid product.

Treating Fraction I with water yielded 5.4 g (34.8% of the theoretical, based on the reacted bromine) of β-bromodihydropyran, with a b.p. of 50-52° at 14 mm.

n_D^{20} 1.5111; d_{20}^{20} 1.5375 (figures given in the literature: b.p. 65° at 25 mm; n_D^{18} 1.5119; d_{18}^{18} 1.5400 [7]). Strongly positive Beilstein reaction. It quickly decolorized a chloroform solution of bromine. Conc. hydrochloric acid was added to its aqueous solution, and the solution was repeatedly evaporated (on a water bath) until all the HCl had been eliminated. Phenylhydrazine was added to the residue, dissolved in alcohol. This yielded 10.4 g of phenylhydrazine phosphite ($H_3PO_3 \cdot H_2NNHC_6H_5$), the equivalent of 7.6 g of diethylphosphoric acid. M.p. 118° (from alcohol) [8].

Fraction II (b.p. 112-116° at 5 mm) boiled in a wide range when redistilled in vacuo. No ethyl ester of α-phosphono-β-bromotetrahydropyran was recovered.

Action of β-bromodihydropyran on triethyl phosphite. 2.1 g of β-bromodihydropyran (b.p. 50-52° at 14 mm) was added to 2.8 g of triethyl phosphite heated to 150-155°. Heating was continued for 2 hours at 155-160°. The initial substance was recovered.

Action of α-epichlorohydrin on triethyl phosphite. 5.3 g of α-epichlorohydrin (b.p. 115-117°; n_D^{20} 1.4385; d_{20}^{20} 1.1833) was added to 10 g of triethyl phosphite, heated to 140°. Heating was continued for 2 hours at 140-150°. The initial substances were recovered, plus reaction products that had a wide boiling range. None of the ethyl ester of α-epiphosphonohydrin was obtained.

Action of α-epiiodohydrin on triethyl phosphite. 6.8 g of α-epiiodohydrin (b.p. 61-63° at 25 mm; n_D^{20} 1.5450; d_{20}^{20} 2.0388 [9]) was added drop by drop during the course of 15 minutes to 8 g of triethyl phosphite (6.13 g being called for theoretically), heated to 140-150°. Heating at 155-165° was continued for 20 minutes (until no more ethyl iodide was driven off.)

The ethyl ester of α-phosphono-β,γ-epoxypropane distilled at 130-132° and 11 mm as a colorless, oily liquid that was readily soluble in water; n_D^{20} 1.4394; 3.4 g (47.7% of the theoretical). Upon redistillation the ester distilled at 131-133° at 13 mm.

n_D^{20} 1.4405; d_4^{20} 1.1373.

0.0900 g subs.: 27.0 ml NaOH (T = 0.0191). Found %: P 15.87. $C_5H_{11}O_4P$. Calc. %: P 15.97.

Hydrolysis of the ester. 0.9 g of the substance was heated to boiling for 4 hours with 1 g of NaOH in 50 ml of H_2O. This yielded 0.63 g of a thick noncrystallizing liquid. Its Ba salt was analyzed:

0.2404 g subs.: 0.1380 g $BaSO_4$. Found %: Ba 33.78. $(C_5H_9OCH_2PO_3OH)_2Ba$.

Calculated %: Ba 33.39. $(CH_2OHCHOHCH_2P(=O)(OH)-O-)_2Ba$. Calculated %: Ba 30.7.

Action of 4-Chloromethyldioxolan-1,3 on triethyl phosphite and sodium diethylphosphite. 1) 1.7 g of triethyl phosphite (8.13 g being called for) and 6 g of the chloride (b.p. 54-56° at 23 mm; n_D^{20} 1.4500; d_4^{20} 1.2468 [10]) were heated to 145-152° for 6 hours. Vacuum distillation (at 36 mm) yielded 10.7 g of a mixture of the initial substances, with a b.p. of 63-73°. The residue was an oily liquid. The experiment was continued by heating the 10.7 g to 220-230° in a sealed tube for 6 hours. The reaction product was decanted from the residue. Upon redistillation in vacuo the ethyl ester of 4-phosphonomethyldioxolan-1,3 distilled at 120-121° at 3.5 mm as an oily liquid that was readily water-soluble. It weighed 2.3 g (24.3% of the theoretical).

n_D^{20} 1.4440; d_4^{20} 1.1716. 0.0824 g subs.: 17.04 ml NaOH (T = 0.0244). 0.0560 g subs.: 11.3 ml NaOH. Found %: P 13.97, 13.63. $C_5H_{11}O_5P$. Calculated %: P 13.83.

2) 10 g of the chloride was added to a benzene solution of sodium diethylphosphite (13.3 g of diethylphosphorous acid and 1.9 g of metallic sodium in 50 ml of anhydrous benzene), and the mixture was heated for 8 hours to the boiling point of benzene. Traces of sodium chloride settled out. The ethyl ester of 4-phosphonomethyldioxolan-1,3 was not secured.

Action of 4-chloromethyl-2,2-dimethyldioxolan-1,3 on triethyl phosphite. 9 g of triethyl phosphite (9.92 g being called for theoretically) was heated to 157-164° for 30 hours* with 9 g of the chloride (b.p. 155-157°; n_D^{20} 1.4358; d_4^{20} 1.1067 [11]).

The ethyl ester of 4-phosphonomethyl-2,2-dimethyldioxolan-1,3 distilled at 117-119° and 4 mm as an oily liquid that was readily water-soluble. The yield was 2 g (14.6% of the theoretical).

n_D^{20} 1.4380; d_4^{20} 1.1029.

0.0728 g subs.: 13.86 ml NaOH (T = 0.02392). Found %: P 12.60. $C_7H_{15}H_5P$. Calc. %: P 12.30.

Hydrolysis of the ester. 1.2 g of the substance was heated to boiling with 0.6 g of NaOH in 50 ml of water and then distilled after another 50 ml of water had been added. The aqueous distillate was boiled for 15 minutes with 0.1 g of 2,4-dinitrophenylhydrazine. The next day the crystals of the dinitrophenylhydrazone of acetone were filtered out. M.p. 126° after recrystallization from alcohol; mixed melting point 126°. The residue left after the acetone had been driven off yielded 0.7 g of β,γ-dihydroxypropylphosphinic acid as a thick liquid. Its barium salt was analyzed.

0.5704 g substance: 0.2970 g $BaSO_4$. Found %: Ba 30.64. $(CH_2OHCHOHCH_2-PO_2OH)_2Ba$. Calculated %: Ba 30.70

Action of 4-chloromethyl-2-phenyldioxolan-1,3 on triethyl phosphite. 8.4 grams of triethyl phosphite (7.86 g being called for theoretically) and 9.4 g of the chloride (b.p. 147-148° at 16 mm; n_D^{20} 1.5330; d_4^{20} 1.2211 [10] were heated together for 12 hours, the temperature being gradually raised from 172° to 197°.

The ethyl ester of 4-phosphonomethyl-2-phenyldioxolan-1,3 distilled at 186-188° at 3 mm; n_D^{20} 1.5014; 5.4 g (38% of the theoretical). The ester redistilled at 184-186° at 3 mm.

n_D^{20} 1.4498; d_4^{20} 1.1737.

0.0836 g substance: 13.19 ml NaOH (T = 0.02392). Found %: P 10.45. $C_{12}H_{17}O_5P$. Calculated %: P 10.33.

Hydrolysis of the ester. 1.2 grams of the substance was refluxed for 4 hours with 0.8 g of NaOH in 50 ml of

* All the experiments with dixolan were run in an Arbuzov flask with a tall tube sealed on it. The triethyl phosphite that distilled over was periodically poured back into the reaction flask.

water. The benzaldehyde was extracted with ether. We secured 0.3 g of the phenylhydrazone (equivalent to 38% of the benzaldehyde) with an m.p. of 155°. Its mixed melting point was the same. The residue yielded 0.5 g of β,γ-dihydroxypropylphosphinic acid. Its barium salt was analyzed.

0.6738 g substance: 0.3591 $BaSO_4$. Found %: Ba 31.35. $C_6H_{15}O_5P_2Ba$. Calculated %: Ba 30.70.

Action of 4-chloromethyl-2-anisyldioxolan-1,3 on triethyl phosphite. Synthesis of 4-chloromethyl-2-anisyldioxolan-1,3: 15 g of anisaldehyde and 14 g of α-chlorohydrin were heated together for 30 hours on an oil bath at 100-125°. 8 grams of the chloride was obtained. B. p. 168-171° at 5 mm.

n_D^{20} 1.5394; d_{20}^{20} 1.2465.

0.1154 g substance: 0.0690 AgCl (Carius). Found %: Cl 14.79. $C_{11}H_{13}O_3Cl$. Calculated %: Cl 15.53.

6.3 grams of triethyl phosphite (5 g being called for theoretically) and 6.9 g of the chloride were heated together for 15 hours, the temperature being gradually raised from 165 to 205°.

The ethyl ester of 4-phosphonomethyl-2-anisyldioxolan-1,3 distilled at 229-231° at 5 mm as a water-insoluble thick liquid. The yield was 4 g (40 % of the theoretical).

n_D^{20} 1.5065; d_{20}^{20} 1.1935. 0.0974 g substance: 14.36 ml NaOH (T - 0.02392) Found %: P 9.76. $C_8H_{17}O_6P$. Calculated %: P 9.39.

Hydrolysis of the ester. 1.5 grams of the substance was heated to boiling with 0.9 g of NaOH in 50 ml of water, anisaldehyde being driven off (after 50 ml more of water had been added). We obtained 0.8 g of the phenylhydrazone with an m.p. of 120-121° (equivalent to 77.4% of anisaldehyde). After the aldehyde had been driven off, the residue yielded 0.8 g of β,γ-dihydroxypropylphosphinic acid.

0.7882 g Ba-salt. Taken $BaSO_4$. 0.4074 g. Found %: Ba 30.42. $C_6H_{15}O_5P_2Ba$. Calculated %: Ba 30.70.

SUMMARY

Representatives of the esters of phosphinic acids with heterocyclic radicals that contain 1 or 2 oxygen atoms have been synthesized for the first time by the action of triethyl phosphite or sodium diethylphosphite upon the respective halogen derivatives.

Esters of phosphinic acids containing a three-membered, five-membered, or a six-membered heterocyclic ring with a single oxygen atom and a five-membered dioxolan ring containing two oxygen atoms have been synthesized.

The synthesized esters have been saponified.

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SYNTHESIS OF ESTERS OF PHOSPHINIC ACIDS THAT CONTAIN HETEROCYCLIC RADICALS

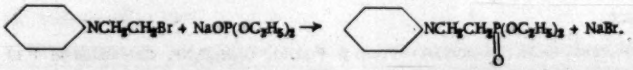
III. THE ACTION OF SODIUM DIETHYLPHOSPHITE AND TRIETHYL PHOSPHITE ON SOME HALOGEN DERIVATIVES OF PYRIDINE AND PIPERIDINE

B. A. Arbuzov and B. P. Lugovkin

In our previous reports we described the results of synthesizing esters of phosphinic acids that contain thiazole radicals [1] and heterocyclic radicals with one or two atoms of oxygen in the ring [2].

In the present report we cite our findings on the synthesis of phosphinic acids and of their esters that contain a piperidine ring and report on our efforts to introduce the diethylphosphono group into the pyridine ring, which have been unsuccessful thus far.

The action of sodium diethylphosphite upon N-(β-brombethylpiperidine readily yielded the ethyl ester of N-(β-phosphonoethyl)-piperidine, the yield being 56.8% of the theoretical.



Saponifying the ester with hydrochloric acid yielded N-(β-phosphonoethyl)-piperidine hydrochloride; reacting the ethyl ester of N-(β-phosphonoethyl)-piperidine with ethyl bromide yielded the crystalline ethobromide, while reacting it with ethyl iodide yielded the ethiodide.

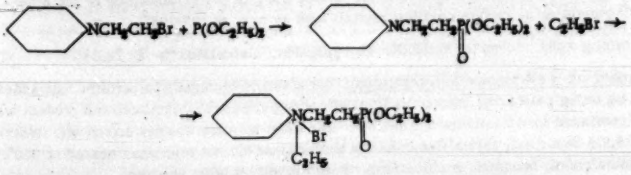
Similarly, 52.6% of the theoretical yield of the ethyl ester of N-(γ-phosphonopropyl)-piperidine

was produced by reacting N-(γ-bromopropyl)-piperidine with sodium diethylphosphite.

Reacting the ethyl ester of N-(γ-phosphonopropyl)-piperidine with ethyl iodide yielded the ethiodide, with an m.p. of 83-84°. The ethobromide is a noncrystallizing oil.

It is worthy of note that our attempts to secure the esters of N-(β-phosphonoethyl)-piperidine and N-(γ-phosphonopropyl)-piperidine by reacting the respective bromides with triethyl phosphite met with failure.

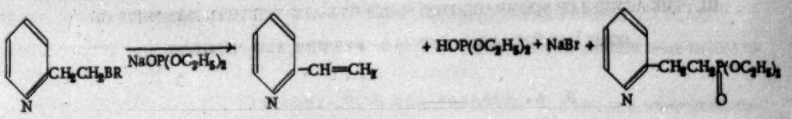
The course of the reaction may be depicted as follows:



The ethyl bromide produced during the reaction might result in the formation of the ethobromide which we secured from N-(β-diethylphosphonoethyl)-piperidine and ethyl bromide.

The reaction between N-(β-bromoethyl)-piperidine and triethyl phosphite resulted in the synthesis of a crystalline product that did not fuse up to 350° and had nothing in common with the ethobromide of the normal reaction product. The state of affairs was similar when we reacted N-(γ-bromopropyl)-piperidine with triethyl phosphite, a product with an m.p. of 254-258° being secured. We did not determine the structure of the resultant products.

Our attempts to introduce the phosphono group by reacting α-bromo- or α-iodopyridine with sodium diethylphosphite were unsuccessful. These halogen derivatives did not react with sodium diethylphosphite. When 2-(β-bromoethyl)-pyridine was reacted with sodium diethylphosphite, the reaction yielded as its principal product α-vinylpyridine. Besides the α-vinylpyridine, we secured a small fraction, the analysis of which was close to that of the ethyl ester of 2-(β-phosphonoethyl)-pyridine.



EXPERIMENTAL

Action of sodium diethylphosphite on N-(β-bromoethyl)-piperidine. An ether solution of 20.3 g of bromoethylpiperidine [3] in 10 ml of anhydrous ether was added to an ether solution of sodium diethylphosphite, prepared from 15.7 g of diethylphosphorous acid (14.7 g being called for theoretically) and 2.6 g of metallic sodium in 150 ml of anhydrous ether. After 4 hours of boiling, the 8.8 g of precipitated sodium bromide (11 g being called for) was filtered out and washed with anhydrous ether, the ether being driven off, and the reaction product being distilled in vacuo. When redistilled in vacuo, the ethyl ester of N-(β-phosphonoethyl)-piperidine distilled at 123-125° at 2 mm as an oily substance, readily soluble in water. The yield was 15 g or 56.8% of the theoretical.

n_D^{20} 1.4615; d_{20}^{20} 1.0438.

0.0858 g substance: 15.12 ml NaOH (T = 0.02442). Found %: P 11.91. $C_{11}H_{24}O_3NP$. Calculated %: P 12.44.

Hydrolysis. 3.2 grams of the ether was heated to 110-115° for 6 hours in a sealed tube together with 24 ml of dilute hydrochloric acid (1:1). The solution was thoroughly boiled with activated charcoal and repeatedly evaporated on a water bath to eliminate the HCl completely, drying at 120-135° yielding 3 g of N-(β-phosphonoethyl)-piperidine hydrochloride as minute crystals with an m.p. of 168-171°. The m.p. was 170-172° after precipitation with anhydrous ether from absolute alcohol.

0.1490 g substance: 28.5 ml NaOH (T = 0.02442). 0.1148 g substance: 0.0730 g AgCl. Found %: P 12.98; Cl 15.73. $C_7H_{16}O_3NP \cdot HCl$. Calculated %: P 13.50; Cl 15.46.

Action of ethyl iodide and bromide. 0.7 gram of ethyl iodide (an excess) was added to 0.6 g of the ester of N-(β-phosphonoethyl)-piperidine. Crystals settled out the next day. Washing with anhydrous ether yielded 0.7 g of the ethiodide of the ethyl ester of N-(β-phosphonoethyl)-piperidine, with an m.p. of 161-162°. The m.p. was 163° after precipitation from absolute alcohol with anhydrous ether. It was readily soluble in water and in alcohol, though insoluble in ether.

0.1190 g substance: 0.0692 g AgI. Found %: I 31.48. $C_{13}H_{29}O_3NPI$. Calculated %: I 31.35.

2 grams of ethyl bromide (an excess) was added to 1.3 g of the ester. The crystals that settled out were filtered out a few days later and washed with anhydrous ether. This yielded 0.5 g of the ethobromide of the ether ester of N-(β-phosphonoethyl)-piperidine as minute colorless crystals with an m.p. of 127-128°.

0.0350 g substance: 0.0187 g AgBr. Found %: Br 22.76. $C_{13}H_{29}O_3NPBr$. Calculated %: Br 22.34.

Action of triethyl phosphite on N-(β-bromoethyl)-piperidine. 6.3 grams of bromoethylpiperidine was added to 7 g of triethyl phosphite (5.44 g being called for), heated to 120-130° (within the flask). The reaction product was a colorless solid. Heating was continued for 15 minutes at 130-150°. The ethyl bromide was not driven off. Washing with anhydrous ether yielded 8.2 g of a finely crystalline colorless product that did not fuse when heated to 350°. It was insoluble in ether, absolute alcohol, benzene, or chloroform, though readily soluble in water.

The ether solution yielded 3.6 g of a liquid product with the odor of triethyl phosphite. No ethyl ester of N-(β-phosphonoethyl)-piperidine was recovered [cf. the experiment with N-(γ-bromopropyl)-piperidine].

Analysis of the solid:

0.0799 g, 0.0742 g substance: 3.74 ml, 3.76 ml NaOH [1]. 0.0988 g, 0.0972 g substance: 0.0810 g, 0.0822 g AgBr (Carius). Found %: P 3.17, 3.43; Br 34.89, 35.99. $(C_7H_{14}NBr)_4 \cdot P(OC_2H_5)_3$. Calculated %: P 3.31; Br 34.26.

Hydrolysis. 1.5 g of the substance was dissolved in 15 ml of water and refluxed for 13 hours. 0.9 grams of NaOH was added plus an additional 20 ml of water, after which the whole was distilled. At the start of distillation an oily product passed over. Acidulation of the distillate with hydrochloric acid and evaporation to dryness yielded 1.2 g of a solid brown residue. Recrystallization from absolute alcohol yielded 0.3 g of a colorless crystalline hydrochloride that did not fuse when heated to 230° (the melting point of N-(β-hydroxyethyl)-piperidine hydrochloride is 120° [4]).

The aqueous residue was acidulated with hydrochloric acid and repeatedly evaporated until all the HCl had been eliminated; re-extraction with absolute alcohol then yielded a thick liquid. When this liquid was reacted with an alcoholic solution of phenylhydrazine, a crystalline product settled out (as much as 0.6 g). The m.p. was 117-118° with softening after recrystallization from alcohol; its mixed melting point with synthesized phenylhydrazine phosphite (m.p. 118°) exhibited a depression: m.p. 102-103°.

0.0592 g substance: 1.65 ml NaOH. Found %: P 1.88.

Action of sodium diethylphosphite on N-(γ-bromopropyl)-piperidine. An ether solution of 14 g of bromopropylpiperidine [5] in 10 ml of anhydrous ether was added to an ether solution of sodium diethylphosphite, prepared from 10.4 g of diethylphosphorous acid (9.37 g being called for) and 1.8 g of metallic sodium in 150 ml of anhydrous ether. After 6 hours of boiling, the precipitated sodium bromide was filtered out and washed with anhydrous ether. The ether was driven off, and the residue distilled in vacuo. The ethyl ester of N-(γ-phosphonopropyl)-piperidine distilled at 135-137° and 3 mm as an oily liquid, readily soluble in water. The yield was 9.4 g, or 52.6% of the theoretical. The b.p. was 136-137° at 3 mm after redistillation:

n_D^{20} 1.4602; d_{20}^{20} 1.0243.

0.0534 g substance: 9.76 ml NaOH. Found %: P 12.36. $C_{12}H_{26}O_3NP$. Calculated %: P 11.78.

Hydrolysis. 2.5 grams of the ester was heated to 100-115° in a sealed tube for 6 hours together with 16 ml of dilute hydrochloric acid (1:1). The solution was thoroughly boiled with activated charcoal. Appropriate processing (cf. the preceding experiment) yielded 2.4 g of N-(γ-phosphonopropyl)-piperidine hydrochloride as minute, faintly yellow crystals with an m.p. of 152-153°. Colorless crystals with an m.p. of 158-159° after precipitation by anhydrous ether from absolute alcohol.

0.1116 g substance: 19.74 ml NaOH. 0.1054 g substance: 0.0650 g AgCl. Found %: P 11.97; Cl 15.25. $C_9H_{21}NPO_3HCl$. Calculated %: P 12.73; Cl 14.58.

Action of ethyl iodide and bromide. 0.6 gram of ethyl iodide (an excess) was added to 0.8 g of the ester of N-(γ-phosphonopropyl)-piperidine. The precipitated oil crystallized several days later. Washing with anhydrous ether yielded 0.9 g of the ethiodide of the ethyl ester of N-(γ-phosphonopropyl)-piperidine, with an m.p. of 82-84°. The m.p. was 83-84° after rewashing with anhydrous ether. The ethiodide settled out as an oil when reprecipitated by anhydrous ether from absolute alcohol.

Analysis of the crystals with an m.p. of 83-84°:

0.1776 g substance: 0.1020 g AgI. Found %: I 31.04. $C_{13}H_{31}O_3NPI$. Calculated %: I 30.31.

0.4 gram of ethyl bromide was added to 0.6 g of the ester. The ethobromide settled out as a noncrystallizing oil. The experiment was repeated, heating the mixture to 85-95° for 2 hours. The ethobromide of the ethyl ester of N-(γ-phosphonopropyl)-piperidine also settled out as a thick oil.

Action of triethyl phosphite on N-(γ-bromopropyl)-piperidine. 4.5 grams of bromopropylpiperidine was added to 4.4 g of triethyl phosphite (3.62 g being called for theoretically), a small quantity of a solid product settling out. The amount of the product increased when the mixture was heated to 100°; when the temperature was raised to 140-155°, the whole reaction mixture consituted a thick liquid. Heating lasted 30 minutes. The ethyl bromide was not driven off. After the reaction mixture had cooled, the reaction mixture solidified when anhydrous ether was added. This yielded 4.5 g of a finely crystalline product (after washing with anhydrous ether). The product was dissolved in absolute alcohol and was precipitated by anhydrous ether. This yielded 3.3 g of a finely crystalline

[1] The titer of the alkali was the same (0.02442).

substance with an m.p. of 254-258° (block), insoluble in anhydrous ether, though soluble in alcohol and in water.

0.1964 g, 0.2096 g substance: 5.28 ml, 6.58 ml NaOH. 0.1160 g, 0.1252 g substance: AgBr 0.0912 g, 0.0940 g (Carius). Found %: P 1.80, 2.11; Br 33.45, 31.95.

The liquid product recovered from the ether solution (obtained in precipitating and washing the solid product) after the ether had been driven off was distilled in vacuo.

Fraction I, with a b.p. of 51-52° at 15 mm. The unreacted triethyl phosphite;[1] n_D^{20} 1.4135 (2.1 g, or 58% of the theoretical).

Fraction II, with a b.p. of 131° at 2 mm. Ethyl ester of N-(γ-phosphonopropyl)-piperidine (with a negligible amount of a solid product); n_D^{20} 1.4358; 0.5 g, or 8.7% of the theoretical.

0.0600 g substance: 9.75 ml NaOH. Found %: P 11.0. $C_{12}H_{26}O_3NP$: Calculated %: P 11.78.

Action of sodium diethylphosphite on α-bromopyridine and α-iodopyridine. I. 4.7 grams of α-bromopyridine, b.p. 75-78°(16 mm); n_D^{20} 1.5709 [6]) was added to a benzene solution of sodium diethylphosphite, prepared from 4.4 g of diethylphosphorous acid and 0.7 g of metallic sodium in 35 ml of anhydrous benzene. When the benzene solution was boiled for 8 hours, a negligible quantity of sodium bromide settled out. No ethyl ester of α-phosphonopyridine was obtained by distillation in vacuo.

II. 13.2 grams of α-iodopyridine (b.p. 97° at 16 mm; n_D^{20} 1.6342; d_4^{20} 1.9281 [7]), was added to a benzene solution of sodium diethylphosphite, prepared from 10 g of diethyl-phosphorous acid and 1.5 g of metallic sodium in 50 ml of anhydrous benzene. When the solution was boiled for 18 hours, a minute quantity of sodium iodide settled out. No ethyl ester of α-phosphonopyridine was secured by distillation in vacuo.

Action of sodium diethylphosphite on β-bromo-2-ethylpyridine. 3.5 grams of bromoethylpyridine (steam-distilled [8]) was added to an ether solution of sodium diethylphosphite, prepared from 2.6 g of diethylphosphorous acid and 0.43 g of metallic sodium in 30 ml of anhydrous ether. The reaction mass was then boiled for 3 hours. 2.3 grams of a solid product settled out, from which 0.6 g of sodium bromide [2])(1.92 g being called for) was extracted by heating the product with a mixture of anhydrous acetone and absolute alcohol. Two fractions were secured by distillation in vacuo after the ether had been driven off.

Fraction I, with a b.p. of 50-55° at 4 mm – 1.3 g. A colorless liquid, water-soluble, with the odor of pyridine bases; n_D^{20} 1.5190; d_4^{20} 0.9976; d_4^{4} 1.0156; it was α-vinylpyridine, contaminated with diethylphosphorous acid. The diethylphosphorous acid was determined by analyzing for phosphorous: 7 ml of NaOH (1 ml being equivalent to 0.0008863 g of P) was required to titrate 0.1173 g of the substance, which was equivalent to 0.3 g of diethylphosphorous acid. 1 gram of the α-vinylpyridine distilled, or 505.5% of the theoretical yield.

The action of auric chloride dissolved in hydrochloric acid yielded α-vinyl chloraurate as minute golden-yellow needles, whose m.p. was 144° after recrystallization from water. An ether solution yielded the picrate as minute yellow needles. The picrate m.p. was 157-158° after recrystallization from alcohol. The constants of α-vinylpyridine are given as follows in the literature: b.p. 79-82° at 29 mm; d_4^{4} 0.9985. The m.p. of the chloraurate ($C_7H_7 \cdot HCl \cdot AuCl_3$) is 144° [9].

Fraction II, with a b.p. of 150-153° at 5 mm, weight 0.7 g. An oily, water-soluble liquid containing a minute amount of a solid product n_D^{20} 1.5020; d_4^{20} 1.1290. Found %: P 11.3; calculated % (for the ethyl ester of β-phosphono-2-ethylpyridine): P 12.75. We were unable to isolate the ethyl ester of β-phosphono-2-ethylpyridine in the pure state because of the small amount of the fraction.

SUMMARY

1. The ethyl esters of N-(β-phosphonoethyl)-piperidine and N-(γ-phosphonopropyl)-piperidine have been synthesized by reacting N-(β-bromoethyl)-piperidine and N-(γ-bromopropyl)-piperidine with sodium diethylphosphite. The hydrochlorides of the respective acids have been secured by saponifying the esters.

2. The action of triethyl phosphite on N-(β-bromoethyl)-piperidine and N-(γ-bromopropyl)-piperidine does not yield the expected esters, N-(β-phosphonoethyl)-piperidine and N-(γ-phosphonopropyl)-piperidine, respectively.

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1) The boiling point of triethyl phosphite is 49° at 12 mm; n_D^{20} 1.4135.

2) Part of the sodium bromide dissolved in the acetone-alcohol mixture.

High melting substances of unknown structure are produced.

3. α-Bromo- and α-iodopyridines do not react with sodium diethylphosphite. The principal reaction product of the reaction between 2-(β-bromoethyl)-pyridine and sodium diethylphosphite is α-vinylpyridine.

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ABSORPTION SPECTRA AND FINE STRUCTURE OF THE SUBSTITUTION DERIVATIVES OF QUINOLINE, THE INITIAL SUBSTANCES FOR ANTIMALARIALS

I. THE TAUTOMERISM OF THE ISOMERIC 2- AND 4-AMINOPYRIDINES

V. I. Bliznyukov

The 2- and 4-aminopyridines differ considerably from the isomeric 3-aminopyridine chemically; they are not diazotized under ordinary conditions, for example, nor do they form salts with 2 equivalents of HCl, though the 3-isomer does. Tautomerism is usually cited as the reason for these and other differences. It is proved in the present spectographic research that there is no tautomerism for the 2- and 4-aminopyridines. The ring nitrogen (meta-orienting) and the amino group interact more or less, depending upon the nature of the solvent and the medium, the interrelationship that is established resembling that occurring with nitroaniline, hydroxybenzaldehyde, etc. The spectra exhibit absorption bands that are typical of ortho and para substituted derivatives, while the bands that are typical of the tautomeric imino form of the aminopyridines is not found.

We undertook the study of the isomeric 2- and 4-aminopyridines in connection with spectrographic research on the antimalarial properties of quinoline derivatives in which a diethylaminoalkyl group has been substituted at the 4 or 2 position. The latter presented great difficulty in selecting the spectra of the principal compound: 6-methoxy-4-(δ-diethylamino-α-methylbutyl)-aminoquinoline. We made a study of the spectra of 6-methoxy-4-aminoquinoline, 4-aminoquinoline, and the isomeric 2- and 4- aminopyridines in order to interpret them correctly. We start out with the simplest: 4-aminopyridine.

E. Braude was the first to investigate the absorption spectra of 4-aminopyridine in 1947, his results being published casually in a study of the products formed in the reaction of acetamidobenzene-sulfanilazide with pyridine [1]. It is noted that the spectrum of 4-aminopyridine in n-amyl alcohol and in aqueous solutions of hydrogen chloride has one high-intensity absorption band, while its spectrum in concentrated sulfuric acid resembles that of pyridine.

One distinct absorption band with a maximum of approximately λ2440 Å is found for 4-aminopyridine in ethyl alcohol solution. The absorption spectrum is hardly displaced at all in an alcoholic hydrochloric solution, but another band with a maximum at λ2600 Å appears, together with a very low minimum, separating it from the short-wave region [2].

The absorption spectrum of 4-aminopyridine in a dioxane-water solution (72%: 28%) has a single absorption spectrum with a maximum at about λ2610 Å. [3].

We made a more thorough investigation of 4-aminopyridine in hexane, alcohol, water, glycol, dichloroethane, and chloroform in the presence of alcoholic solutions of HCl of various strengths, in 72% $HClO_4$, in concentrated H_2SO_4, and in solutions of sodium alcoholate. In our research we used 4-aminopyridine secured from pyridine via 4-pyridyl-pyridinium dihydrochloride and treating the latter with ammonia [4]. Colorless white crystals with an m.p. of 159° after recrystallization from water and then from heptane. The figures given in the literature are: m.p. 157-158° [2], 150° [3], and 159-160° [5].

4-Aminopyridine in neutral solutions. 4-Aminopyridine dissolved with great difficulty in hexane. We were able to begin our investigation at the concentration of $2 \cdot 10^{-4}$ mole. The absorption spectrum has two absorption bands, one with a maximum at approximately λ 2550 Å* and ε 8000 and the other a distinct band with a maximum at λ2295 Å and ε40000.

A comparison of the absorption spectrum curves of 4-aminopyridine in hexane and in dichloroethane with the spectrum of aniline in hexane (Fig. 1, Curves 1, 4, and 10) shows their similarity in the far ultraviolet, whenever the only difference between the maxima at approximately λ2300 Å is their intensity. The absorption

* The mean point of the extended curve was taken.

band for aniline in the middle ultraviolet, with a maximum at λ 2845 Å is not found in the 4-aminopyridine curve, possibly because of its lower intensity and its displacement toward the shorter wave-lengths. The aniline band with a maximum at λ 2845 Å is fairly close to the bend in the curve of the 4-dimethylaminopyridine substituted on the amino group in dioxane (Fig. 1, Curve 9).

The absorption curve of 4-aminopyridine in hexane, with a maximum at λ 2550 Å, may correspond to the pyridine band with a maximum at λ 2520 Å, log ε 3.4 for pyridine (Fig. 1, Curves 1 and 6). Table 1 below collates the maxima of the absorption bands of 4-aminopyridine, pyridine, and aniline in hexane.

TABLE 1

Compound	First aniline band		Pyridine band		Second aniline band	
	λ	ε	λ	ε	λ	ε
4-Aminopyridine in hexane	–	–	2550[1]	3000	2295	40000
4-Aminopyridine in dichloroethane	–	–	2550	3500	2365	12500
4-Dimethylaminopyridine in dioxane-water solution (72%; 28%) (Anderson)	2900[1]	2000	?	?	2580	25000
Aniline in hexane (Klingstedt)	2845	1470	–	–	2340	6800
Pyridine in hexane	–	–	2530	2000	–	–

1) The mean point of the extended curve was taken.

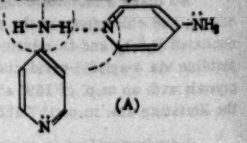
Thus, there is one absorption band, in the far ultraviolet, in the spectrum of a nondipole hexane solution of 4-aminopyridine. The same sort of band is found in aniline. This signifies that ring nitrogen plays no part herein, so that the same conditions are present for the reaction of the NH_2 group with the ring as exist in aniline.

Another absorption band is found in the spectrum of the same hexane solution of 4-aminopyridine in the middle ultraviolet. There is the same sort of band in pyridine. This means that the NH_2 group plays no part here, so that the same conditions exist for the reaction of nitrogen with the ring as are present in pyridine. If we assume that the molecules of 4-aminopyridine are associated, we may actually have favorable conditions in hexane for the appearance of the above-mentioned aniline and pyridine absorption curves in 4-aminopyridine (Diagram A):

In this diagram of associated 4-aminopyridine (A), the amino group of one molecule is connected by a hydrogen bond with the ring nitrogen of a second and third molecule. As a result, the ability of 4-aminopyridine to exhibit absorption bands in its spectra that are present in aniline and pyridine may be ascribed to the conjugation effect [8], which causes the ring nitrogen to be electron acceptor center in the left-hand portion of the associated aminopyridine, with the NH_2 group being the electron donor center at the right.

The absorption spectra of 4-aminopyridine have been studied in water, glycol, and alcohol at concentrations of $2 \cdot 10^{-6}$ to $2 \cdot 10^{-5}$ mole. When we compare the curve of 4-aminopyridine in water with that in hexane (Fig. 1, Curves 2 and 1) demonstrates that they differ greatly. As a result of dissolution in water, the absorption band of 4-aminopyridine that is called the "pyridine" band does not appear, though we find a new high-intensity band with a maximum of λ 2600 Å and ε 50000. Aniline manifests hardly any band in the far ultraviolet owing to its faintness together with the displacement of the maximum to the visible region.

In glycol 4-aminopyridine exhibited one high-intensity band, exactly like the one in the aqueous solution, with a maximum at λ 2600 Å and a further lowering of the minimum to ε 1000 (Fig. 1, Curves 5 and 1).



(A)

The absorption curve of 4-aminopyridine in alcohol resembles its spectrum in hexane. It is distinguished by the slightly lower intensity of the (second) aniline band in the far ultraviolet and a substantial shift of the maximum of this band toward the visible region by 165 Å. As compared to its curves in water and in glycol, the curve of 4-aminopyridine in alcohol exhibits a slightly more pronounced inflection of the curve in the region where the λ 2600 Å maximum is located and has an aniline absorption curve in the far ultraviolet (Fig. 1, Curve 3 and 1). The data on the band maxima of 4-aminopyridine in water, glycol, alcohol, and hexane are listed in Table 2.

In hexane that contained a minute quantity of water (0.7%), on the basis of 2 moles of water per mole of 4-aminopyridine, with the concentration of the latter totaling $2 \cdot 10^{-4}$ mole, we secured a 4-aminopyridine curve that practically coincided with its curve in anhydrous hexane. We do not reproduce this curve to save space.

In its chemical nature and electron distribution [6] the pyridine nucleus more closely resembles nitrobenzene than benzene. In pyridine derivatives – 2- and 4-chloropyridines – the halogen, for example, is hydrolyzed as readily as in the 2- and 4-chloronitrobenzenes, in contrast to the low reactivity of the halogens in the corresponding

TABLE 2

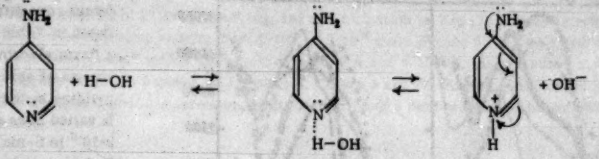
Compound	"Para-band"		Pyridine band		Aniline band	
	λ	ε	λ	ε	λ	ε
4-Aminopyridine in water	2600	50000	–	–	2350•	12000
4-Aminopyridine in glycol	2615	50000	–	–	–	–
4-Aminopyridine in alcohol	2625•	5000	–	–	2460	31000
4-Aminopyridine in hexane	–	–	2550	3000	2295	40000

chlorobenzenes. The resemblance of pyridine and its derivatives to nitrobenzene is also manifest in the inability of the former to enter into substitution reactions when anhydrous aluminum chloride is present.

On the other hand, pyridine and its derivatives act like weak bases [7], when dissolved in water, chloroform, carbon tetrachloride, chlorobenzene, and other solvents, giving a "noncovalent" electron pair of the ring nitrogen to the solvent's molecule.

$$C_5H_5N: + H-OH \rightleftarrows C_5H_5N \ldots H-OH \rightleftarrows [C_5H_5NH]^+OH^-$$

The discovery of an absorption band with a maximum at approximately λ 2600 Å in the spectra of aqueous solutions of 4-aminopyridine may be attributed to the band that is typical of para-substitution derivatives and is explainable as a manifestation of a conjugation effect [8], the "noncovalent" electron pair of the amino group being involved in interaction with the ring nitrogen. This will promote the hydration of the ring and the emergence of a singly-charged cation.



The general shape of the absorption band of 4-aminopyridine that has a maximum at about λ 2600 A reminds one of the typical "para absorption band" of p-nitroaniline or p-nitrophenol or p-hydroxybenzaldehyde, and the like. The spectral absorption curves of these compounds are not reproduced for comparison with the 4-aminopyridine curve, because their "para bands" are greatly shifted toward the visible region. This is attributable to the similarity, but not equivalence, of the nitrogen atom in the ring and, say, the nitro group in the side chain. Hence, the weakening of the (second) aniline band in the far ultraviolet observed when 4-aminopyridine is dissolved in water and in glycol may be attributed to a conjugation effect, the "noncovalent" electron pair of the nitrogen atom in the amino group reacting with the ring nitrogen.

Measurements of the dipole moment likewise indicate the feasibility of the emergency of a "para band" in 4-aminopyridine. 4-Aminopyridine has a $\mu = 4.36$ D [5], which is considerably higher than that calculated from the moments of pyridine and aniline in dioxane (2.22 + 1.90 = 4.12 D).

4-Aminopyridine in alcoholic solutions of HCl, concentrated $HClO_4$, and concentrated H_2SO_4. 4-Aminopyridine dissolved with a concentration of $2 \cdot 10^{-3}$ to $2 \cdot 10^{-4}$ mole in alcohol that contained 0.1 mole of HCl per mole of the substance (Figure 2, Curves 6 and 9) exhibited a complex, wide absorption band with a maximum at approximately λ 2460 A and ε 10000. Compared to the curve in neutral alcohol, the intensity is much greater in the vicinity of the "para band", and there is no aniline. Apparently these bands are superimposed. Such a change in the absorption spectra of 4-aminopyridine in the presence of dilute solutions of HCl of the order of $2 \cdot 10^{-4}$ mole (or about 0.001% HCl) cannot be attributed to the formation of a salt, inasmuch as alcoholysis usually sets in under these conditions. In all probability we have here the combined action of two reagents, the alcohol and the hydrogen chloride; on the ring nitrogen of the 4-aminopyridine, analogous to the action of water noted above, though not as strongly. Increasing the quantity of HCl tenfold brings about the formation of a "para absorption band" with a maximum of λ 2630 A and ε 20000, and a (second) aniline absorption band with a maximum at λ 2490 A and ε 20000 in 4-aminopyridine (dissolved in alcohol containing 1 mole of HCl per mole of the substance) in concentrations ranging from $2 \cdot 10^{-2}$ to $2 \cdot 10^{-4}$ mole (Figure 2, Curves 5, 9, and 6), The minimum separating these bands is very shallow, though the minimum delimiting the aniline absorption band on its short-wave side is deeper, extending to ε 2000. Increasing the amount of HCl to 100 moles of HCl per mole of 4-aminopyridine, with the latter's concentration ranging from $2 \cdot 10^{-3}$ to $2 \cdot 10^{-4}$ (Figure 2, Curve 1) brings forth one high-intensity band, corresponding to a "para band" with a maximum at λ 2630A and ε 60200, and deepens the minimum delimiting this band on its short-wave side to ε 1000. When the concentration of hydrochloric acid is raised from 25,000 to 250,000 moles of

• The mean point of the extended curve was taken.

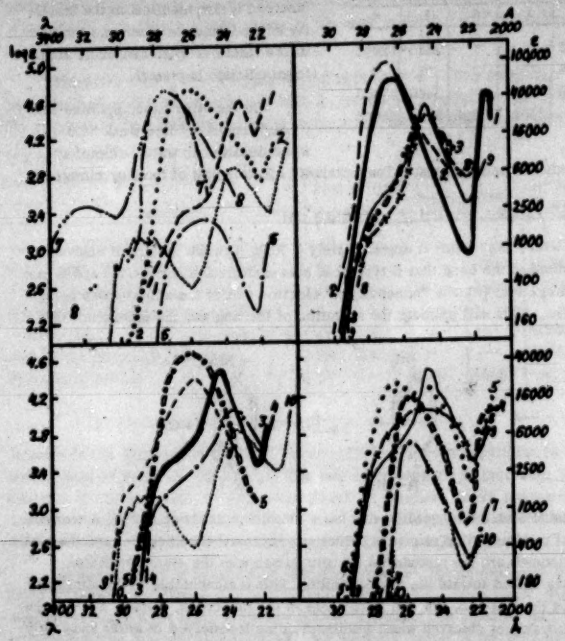


Fig.1

1) 4-aminopyridine in hexane $2 \cdot 10^{-4}$ mole; 2) 4-aminopyridine in water, from $2 \cdot 10^{-3}$ to $2 \cdot 10^{-5}$ mole; 3) 4-aminopyridine in alcohol, from $2 \cdot 10^{-3}$ to $2 \cdot 10^{-5}$ mole; 4) 4-aminopyridine in dichloroethane, from $2 \cdot 10^{-3}$ to $4 \cdot 10^{-4}$ mole; 5) 4-aminopyridine in glycol, from 10^{-3} to $2 \cdot 10^{-4}$ mole; 6) pyridine in hexane; 7) 1-methyl-4-iminopyridine dissolved in 90%: 10% dioxane-water (Anderson); 8) 1-methyl-4-aminopyridine in 72%:28% dioxane-water (Anderson); 9) 4-dimethylaminopyridine dissolved in 90%:10% dioxane-water (Anderson); 10) aniline in hexane (Klingstedt).

Fig. 2.

1) 4-aminopyridine in alcohol, from $2 \cdot 10^{-3}$ to $2 \cdot 10^{-4}$ + 100 moles HCl; 2) 4-aminopyridine in a 5-molar alcoholic solution of HCl, from $2 \cdot 10^{-3}$ to $2 \cdot 10^{-5}$ mole; 3) 4-aminopyridine in 72% (12-molar) $HClO_4$, from $2 \cdot 10^{-3}$ to $2 \cdot 10^{-4}$ mole 5) 4-aminopyridine in alcohol 10^{-3} mole + 1 mole of HCl; 6) 4-aminopyridine in alcohol from $2 \cdot 10^{-3}$ to $2 \cdot 10^{-4}$ mole + 0 1 mole of HCl; 7) 4-aminopyridine in conc (17.5-molar) H_2SO_4 from $2 \cdot 10^{-3}$ to $2 \cdot 10^{-5}$ mole; 8) 4-aminopyridine in alcohol + 100-molar HCl, neutralized with an excess of 100-molar $NaOC_2H_5$ $3 \cdot 10^{-4}$ mole; 9) 4-aminopyridine in neutral alcohol; 10) pyridine in conc H_2SO_4.

HCl (5-molar HCl), practically no change takes place in the absorption spectrum of the 4-aminopyridine. Curves 1 and 2 display the same absorption band, the maximum of which in the spectrum with 100 moles of HCl being somewhat weaker. Moreover, the high transmissibility of the acid solution causes an absorption band to appear in the far ultraviolet with a maximum at λ 2115 A and ϵ 39400, which may be attributed to the ethylenic double bond. The figures on the maxima of 4-aminopyridine in alcoholic solutions of hydrogen chloride containing different concentrations of HCl are listed in Table 3. The presence of a "para absorption band" in the spectra of acid solutions of 4-aminopyridine as the HCl concentration is varied over a wide range, from $2 \cdot 10^{-4}$ to 5-molar solutions of HCl, is evidence that 4-aminopyridine forms a salt only with one equivalent of the acid, notwithstanding the presence of two nitrogen atoms in the 4-aminopyridine molecule.

Marckwald [9] and Meyer [10] also noted that they could not isolate salts with two molecules of the acid when they reacted 4-aminopyridine with fuming HCl, in contrast to the isomeric 3-aminopyridine.

The action of 2 moles of an alcoholic solution of $NaOC_2H_5$ on 4-aminopyridine, the latter's concentration ranging from $2 \cdot 10^{-3}$ to $2 \cdot 10^{-4}$ mole (Figure 2, Curves 3 and 9) and that of a weaker solution of $NaOC_2H_5$ involve a weakening of the "para absorption band" compared to the curve in neutral alcohol, while the minimum delimiting the (second) aniline band on its short-wave side is simultaneously raised from ϵ 3000 to ϵ 6000. This is evidently due to a decrease in the ability of the alcohol to be added to the ring nitrogen or to excite it in an alkaline medium. The reversibility of the transition of the 4-aminopyridine from the acidic solution to the alkaline one was tested as follows: sodium alcoholate in an excess above 100 moles of $NaOC_2H_5$ was added to 4-aminopyridine, dissolved in alcohol containing 100 moles of HCl, in order to neutralize the latter (Figure 2, Curves 8, 3, and 1). The coincidence of the curves (8 and 3) for 4-aminopyridine after the acid had been neutralized by the alconolate and when the $NaOC_2H_5$ acted on the 4-aminopyridine directly is quite satisfactory. Hence, there are no profound changes when 4-aminopyridine interacts with hydrogen chloride.

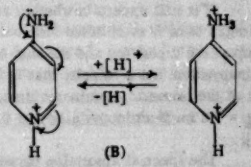
TABLE 3

Compound	"Para-band"		(Second) aniline band		Ethylene band	
	λ	ε	λ	ε	λ	ε
4-Aminopyridine in alcohol containing 0.1 mole HCl.	2460	10000	–	–	–	–
4-Aminopyridine in alcohol containing 1 mole HCl...	2630	20000	2490	20000	–	–
4-Aminopyridine in alcohol containing 100 moles HCl	2630	60200	–	–	2115	40000
4-Aminopyridine in alcohol containing 25,000 to 250,000 moles HCl (in 5-molar HCl).....	2650	100000	–	–	–	–
4-Aminopyridine in neutral alcohol.....	2625	5000	2460	31000	–	–

Our research on 4-aminopyridine was continued with conc.H_2SO_4 (17.5 molar). The spectral absorption curve of 4-aminopyridine in conc.H_2SO_4 precisely repeats the curve for unsubstituted pyridine in conc.H_2SO_4 (Figure 2, Curves 7 and 10), having a single absorption band with a maximum at λ 2550 A and ε 5000.

The fact that the absorption spectrum of 4-aminopyridine in conc.H_2SO_4 turns into that of pyridine may indicate that a salt is produced under these conditions at the amino group, its interaction with the ring being suppressed, while a doubly charged cation is formed (Diagram B).

In contrast to salt formation in 17.5-molar H_2SO_4, the salt formation in 72% (12-molar) chloric acid, with the concentration of the 4-aminopyridine ranging from $2\cdot10^{-3}$ to $2\cdot10^{-4}$ mole (Figure 2, Curves 4 and 7), involves the retention of the "para absorption band" with a maximum at λ 2560 A and ε 16000. As compared with the spectral absorption curve of 4-aminopyridine in 5-molar HCl (Figure 2, Curves 4 and 2), the end of the curve is shifted appreciably toward the ultraviolet, by 100-150 A, resulting in the formation of a doubly charged cation while the singly charged cation is retained.



(B)

2-Aminopyridine in Neutral Solutions

The absorption spectrum of 2-aminopyridine has been investigated [11], one absorption band having been found in neutral and acid solutions. One band with a maximum at λ 2900 A and ε 3800 has also been found for 2-aminopyridine in heptane [12]. When the measurement of the absorption spectrum of 2-aminopyridine in heptane was repeated, one absorption band was again found, with a maximum at λ 2900 A and ε 4000 [13]. When the absorption spectrum of 2-aminopyridine was investigated in alcohol, in a weak acidic medium, and in a weak alkaline medium (0.01 N HCl and 0.01 N NaOH), two absorption bands were found, with maxima at λ 3000-2850 A and ε 6000-4000 and λ 2350-2250 A and ε 12000-10000 respectively [2]; one absorption band with a maximum at λ 3000 A and ε 4450 was found at temperatures of 25, 65, and 80° in a dioxane-water solution (72%: 28%) [3].

We made a more detailed spectrographic study of 2-aminopyridine in hexane, water, alcohol, dichloroethane, and glycol, and in acidic solutions ranging from $2\cdot10^{-4}$ mole HCl to strong 17.5 mole H_2SO_4. We used in our tests a 2-aminopyridine prepared by reacting pyridine with sodamide, as specified by A.E.Chichibabin and Zeide [14]. The 2-aminopyridine was also prepared by reacting 2-bromopyridine with ammonia [15]. The base was refined by distillation in vacuo and recrystallization from petroleum ether. B.p. 57-58. The figure given in the literature is 57-58° [3].

The absorption spectrum of 2-aminopyridine in hexane, at concentrations of 10^{-4} to $2\cdot10^{-3}$ mole exhibits two absorption bands with a maximum at λ 2850A and ε 3000 and a maximum at λ 2300 A and ε 12000, respectively. As we see from a comparison of the absorption spectra curves of 2-aminopyridine and aniline in hexane (Figure 3, Curves 1 and 7), the aniline spectrum is substantially changed without making any allowance for the pyridine absorption band, in contrast to 4-aminopyridine. Adding a minute amount of water to the hexane, namely 2 moles of water per mole of 2-aminopyridine when the latter's concentrations lies between $2\cdot10^{-3}$ and $2\cdot10^{-4}$ (Figure 3, Curves 1 and 2) strengthens the absorption band of the 2-aminopyridine, especially at λ 2850 A. The intensity of these 2-aminopyridine absorption bands is also increased in an aqueous solution, though much less strongly than in hexane that contains a small percentage of water, dissolution in water producing a shift of the 2-aminopyridine curves by 75 A. Water's properties as a solvent are manifested in two ways in this instance: in the substance, i.e., as a strongly associated liquid that reluctantly gives up its own association for association with the molecules of 2-aminopyridine, and in the form of associated molecules, but not in the substance, rather distributed among the

hexane molecules so that there are two molecules of water for every molecule of 2-aminopyridine. That is why the associated molecules of water are more easily dissociated than the molecules of 2-aminopyridine. The rise in the intensity of the 2-aminopyridine absorption bands observed in both instances, compared to their strength in hexane, is evidently the result of the addition of water to the ring nitrogen.

Hence, in contrast to 4-aminopyridine, 2-aminopyridine retains the general nature of its spectrum in hexane and in water, with two absorption bands. This must correspond to an electron distribution like that in the respective ortho substitution derivatives of benzene, and it may be attributed to a conjugation effect produced when the amino group and the ring nitrogen interact, as in o-nitroaniline or o-hydroxybenzaldehyde or o-nitrophenol, and the like.

In contrast to the isomeric 4-aminopyridine, the spectral absorption bands of aniline and pyridine are not found in 2-aminopyridine, most probably because of the superposition of the strongest "ortho absorption bands."

It is still uncertain whether an intramolecular hydrogen bond is established here between the amino group at the 2 position and the ring nitrogen, that 2-aminopyridine has a basicity that is far from the same as that of the isomeric 4-aminopyridine. The literature gives pK_B = 7.2 for 2-aminopyridine and 9.1 for 4-aminopyridine [16].

The spectral absorption curves of 2-aminopyridine in dichloroethane and chloroform lie between the curves in hexane and in water, there being a slight bend in the dichloroethane curve (Figure 3, Curve 5) at about λ 2860 A. The minimum bounding the band on its shortwave side at λ 2250 A rises from ε 6000 to ε 12000 and is shifted somewhat toward the visible region.

The general features of the absorption spectrum curve of 2-aminopyridine in alcohol resemble those of the curve in water (Figure 3, Curves 4 and 3). One difference is the greater depth of the absorption band minima that separate them: the minimum at λ 2550 A drops from ε 600 to ε 300, while the minimum at λ 2200 A drops from ε 6000 to ε 2000. Table 4 gives the figures for the maxima and minima of the absorption curves of 2-aminopyridine in various organic solvents and of aniline in hexane.

The spectral absorption curve of 2-aminopyridine in glycol resembles the curve in water and in alcohol (Figure 3, Curves 6, 3, and 4), the shift of the end of the curve toward the longer wavelengths being greatest and both absorption bands being stronger.

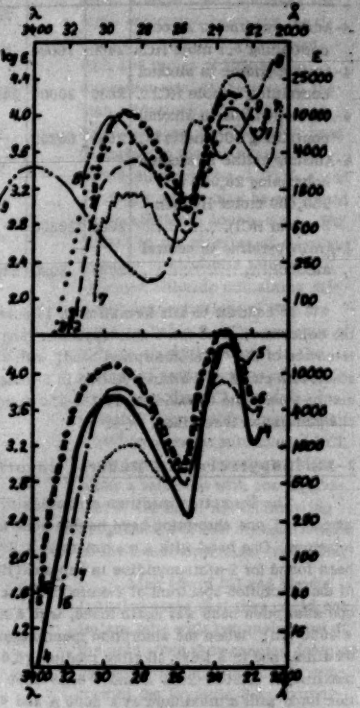


Fig. 3

1) 2-aminopyridine in hexane, from 10^{-3} to $2 \cdot 10^{-3}$ mole; 2) 2-aminopyridine in hexane containing 0.07% H_2O, from $2 \cdot 10^{-3}$ to $2 \cdot 10^{-4}$ mole; 3) 2-aminopyridine in water, from $5 \cdot 10^{-4}$ to $5 \cdot 10^{-3}$ mole; 4) 2-aminopyridine in alcohol, from 10^{-4} to $5 \cdot 10^{-3}$ mole; 5) 2-aminopyridine in dichloroethane, from $5 \cdot 10^{-3}$ to $5 \cdot 10^{-4}$ mole, 6) 2-aminopyridine in glycol, from $2 \cdot 10^{-3}$ to $2 \cdot 10^{-4}$ mole; 7) aniline in hexane (Klingstedt) and in alcohol (Biquard); 8) 1-methyl-2-aminopyridine in alcohol, 10^{-3} mole (Goldfarb); 9) 1-methyl-2-iminopyridine in heptane (Goldfarb).

Thus, the absorption spectrum of 2-aminopyridine has two absorption bands in all the neutral solutions mentioned above, due apparently to an equalization of the electron density, as in ortho substitution derivatives. As for the increase or decrease in the intensity of the individual absorption bands of the "ortho type" when we shift from one neutral solvent to another, this depends upon the varying ability of the ring nitrogen to retain a solvent molecule. As a result, the ring nitrogen becomes more or less positive and, as a meta-orienting factor, exhibits more or less similarity to the nitro group, say, as in o-nitroaniline; that is, the nitrogen and the NH_2 group in 2-aminopyridine can react together more or less readily, this being reflected in the absorption spectra by the emergence of the

TABLE 4

Compound	(First) "ortho-band"				(Second) "ortho-band"			
	Maximum		Minimum		Maximum		Minimum	
	λ	ε	λ	ε	λ	ε	λ	ε
2-Aminopyridine in hexane	2850	3000	2560	600	2300	12000	2180	6000
2-Aminopyridine in hexane with 0.07% H_2O	2900	10000	2545	780	2310	18000	–	–
2-Aminopyridine in water	2940	6000	2520	600	2280	16000	2175	7200
2-Aminopyridine in alcohol	2950	5000	2553	300	2350	20000	2195	2000
2-Aminopyridine in glycol	2955	12000	2575	790	2380	30000	–	–
2-Aminopyridine in dichloroethane	2915	6000	2565	600	2335	20000	2245	12000
Aniline in hexane (Klingstedt)	2845	1470	2600	400	2340	6800	2150	2500

respective "ortho absorption bands".

The 2- and 4-aminopyridines differ greatly from the isomeric 3-aminopyridine, chemically speaking; for example, they are not diazotized under ordinary conditions nor do they produce salts with 2 equivalents of HCl, though the 3-isomer does. The phenomenon of tautomerism is usually cited as an explanation of these differences [17]. Goldfarb, Setkina, and Danyushevsky [13] prepared 1-methyl-2-iminopyridine and investigated it spectrographically while Anderson and Seeger [3] prepared and investigated that as well as methyl-4-iminopyridine as derivatives of the tautomeric imino form. They found that the absorption spectrum for the imino form has two absorption bands, the maxima of 1-methyl-2-iminopyridine in heptane being located at λ 3400 A and ε 2500; and λ 2525 A and ε 3000, while the maxima of 1-methyl-4-iminopyridine in a dioxane–water solution are located at λ 3170 A and ε 2500 and λ 2750 A and ε 50000.

When we compare the spectral absorption curves of 2- and 4-aminopyridines in hexane with the curves of 1-methyl-2-iminopyridine and 1-methyl-4-iminopyridine (Figure 3, Curves 9 and 1; Figure 1, Curves 7 and 1), we find no tautomeric imino form of the 2- and 4-aminopyridines in the absorption spectra we have investigated.

2-Aminopyridine in Alcoholic Solutions of HCl, in Conc. $HClO_4$, and in Conc. H_2SO_4.

The 2-aminopyridine has been studied in alcoholic solutions of hydrogen chloride, starting with weak concentrations of the order of $2\cdot10^{-6}-2\cdot10^{-8}$ mole and ranging up to strong concentrations of 4-mole solutions of HCl. 2-Aminopyridine, dissolved in alcohol containing 0.1 mole of HCl per mole of substance, the concentrations of the latter ranging from $5\cdot10^{-2}$ to $5\cdot10^{-4}$ mole, produced a spectral absorption curve (Figure 4, Curve 3) with two high-intensity absorption bands, a maximum at λ 2935 A and ε 6200 and another at λ 2325 A and ε 18000. As compared with the 2-aminopyridine curve in neutral alcohol, this percentage of HCl (approximately 0.001%) shifts the curve slightly toward the longer wavelengths, intensifies the first absorption band and reduces the depth of the minima of both bands by approximately half. Increasing the percentage of HCl to 10 times what it was before produces an even larger shift of the end of the curve toward the visible region, by about 150 A, and an increase in the intensity of the maxima of both absorption bands for 2-aminopyridine in concentrations of $5\cdot10^{-3}$ to $5\cdot10^{-5}$ mole, with 1 molecule of HCl per molecule of the substance (Figure 4, Curves 2 and 3). The band maximum at λ 2940 A grows much broader in the vicinity of λ 2850 A without any appreciable change occurring in the position of the minimum of this band, while the depth of the minimum of the λ 2325 A band bounding it on the shortwave side is nearly 8 times less. The curve for 2-aminopyridine dissolved in alcohol containing 100 moles of HCl, at concentrations of $5\cdot10^{-4}$ to $5\cdot10^{-6}$ mole (an increase of 100 and 1000 times in the percentage of HCl over the previous figures) generally resembles the curve for 2-aminopyridine in alcohol containing 1 mole of HCl (Figure 4, Curves 1, 3, and 2). The difference is that the λ 2940 A band maximum has a bend at λ 2775 A and ε 6000, corresponding to the previously noted spreading of the maximum of the λ 2940 A absorption band on the curve for 2-aminopyridine in alcohol containing 1 mole of HCl. The minimum that bounds this band on the shortwave side becomes deeper, dropping from ε 600 to ε 300. Table 5 lists the figures on the band maxima and minima for 2-aminopyridine in alcoholic solutions of hydrogen chloride with varying concentrations of HCl.

2-Aminopyridine dissolved in a 4-mole alcoholic solution of HCl, its concentrations ranging from $5\cdot10^{-3}$ to $5\cdot10^{-5}$ mole, yielded a spectral absorption curve that resembled the curve for 2-aminopyridine with 100 molecules of HCl (Figure 4, Curves 4 and 1). Thus, the excitation or salification of 2-aminopyridine is independent of the HCl concentration, the fundamental type of absorption spectrum remaining unchanged.

TABLE 5

Compound	(First) "ortho-band"				(Second) "ortho-band"			
	Maximum		Minimum		Maximum		Minimum	
	λ	ε	λ	ε	λ	ε	λ	ε
2-Aminopyridine in alcohol with 0,1 mole HCl	2935	6200	2560	600	2325	18000	2155	4800
2-Aminopyridine in alcohol with 1 mole HCl	2940	20000	2525	600	2320	40000	2225	30000
2-Aminopyridine in alcohol with 100 moles HCl	3045	18000	2500	300	2335	30000	2230	2000
2-Aminopyridine in neutral alcohol.....	2950	5000	2550	300	2350	20000	2200	20000

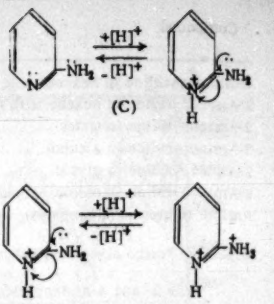


TABLE 6

Compound	(First) "ortho-band"		Pyridine band		(Second) "ortho-band"	
	λ		λ		λ	
2-Aminopyridine in 72% $HClO_4$ (12 mole).....	2965	9000	2590	4500	2270	15800
2-Aminopyridine in 98% H_2SO_4 (17.5 mole)....	2995	200	2533	10000	2375	2200
2-Aminopyridine in 15% HCl (4-mole).....	3075	15800	–	–	2295	39400

The fact that the band in the far ultraviolet grows stronger during the salification of 2-aminopyridine while the depth of the minimum bounding this band on the shortwave side is diminished, is not typical of the aniline absorption band and may correspond to the "ortho bands" of 2-aminopyridine. The shift of the end of the 2-aminopyridine curve by 150 A toward the visible region may be evidence that salt formation involves the ring nitrogen.

The finding of "ortho absorption bands" in the spectra of 2-aminopyridine when the HCl concentration is is changed from the weak 0.001% to 15% indicates that 2-aminopyridine forms a salt with one equivalent of acid, the alcohol and acid probably acting together (Diagram C).

To test the action of more highly concentrated acids upon 2-aminopyridine, in order to discover whether a salt with two equivalents of acid can be formed, we continued our spectrographic research on 2-aminopyridine in conc. sulfuric and chloric acids.

The 2-aminopyridine dissolved in 72% chloric acid (12 moles $HClO_4$) in concentrations from $2 \cdot 10^{-3}$ to $2 \cdot 10^{-5}$ M, exhibited a spectral curve with three absorption bands: a maximum at λ 2965 A and ε 9000, a maximum at λ 2590 A and ε 4500, and a maximum at λ 2270 A and ε 1580. Compared to the curve for 2-aminopyridine in 4M HCl (Figure 4, Curves 6 and 4), the $HClO_4$ weakens the intensity of the wide band with a maximum at λ 2965 A by a factor of 1.6, the end of the curve and the maximum of this band being shifted about 100 A toward the ultraviolet. The minimum on the shortwave side of this band is very shallow, owing to the appearance of a new band with a distinct maximum at λ 2590 A and ε 4500. This band is equivalent to the pyridine band (the maximum λ for pyridine in conc. H_2SO_4 being 2560 A and ε 4500).

In the far ultraviolet the intensity of the second band of 2-aminopyridine is weakened by a factor of 2.5 without any change in the location of the minimum on the shortwave side, though with a great increase in the depth of the minimum on the longwave side. The weakening of the two bands of 2-aminopyridine and the simultaneous appearance of the pyridine band when we shift from the weaker 4M HCl to the stronger 12M $HClO_4$ may be attributed to the passing of some of the 2-aminopyridine molecules into a salt, again at the amino group, the effect of the amino group upon the pyridine ring being suppressed and the pyridine absorption spectrum making its appearance.

We studied 2-aminopyridine in concentrations of $5 \cdot 10^{-4}$ to $5 \cdot 10^{-5}$ in concentrated H_2SO_4 (17.5M), obtaining an absorption spectrum whose appearance differed considerably from that of the curves for 2-aminopyridine in 12M $HClO_4$ and 4M HCl (Figure 4, Curves 5, 6, and 4). The dissolution of 2-aminopyridine in conc. H_2SO_4 greatly weakens the "ortho absorption band" and shifts the end of the curve toward the shorter wavelengths. The (first) "ortho band" in the middle ultraviolet becomes 80 times weaker than the corresponding band in 4M HCl, while the (second)

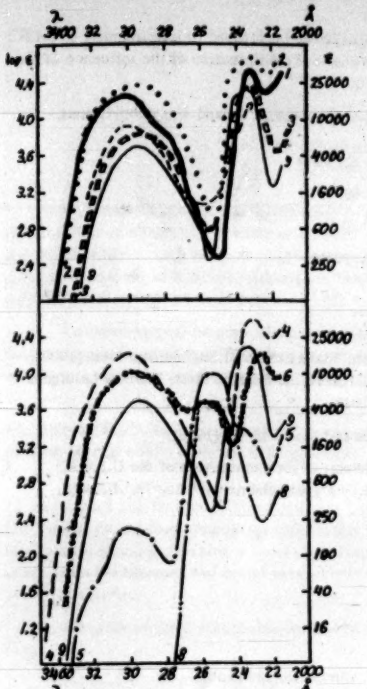


Fig. 4

1 - 2-aminopyridine in alcohol, from $5 \cdot 10^{-2}$ to $5 \cdot 10^{-6}$ M + 100 M. HCl. 2 - 2-aminopyridine in alcohol, from $5 \cdot 10^{-3}$ to $5 \cdot 10^{-5}$ M + 1M. HCl. 3 - 2-aminopyridine in alcohol, from $5 \cdot 10^{-2}$ to $5 \cdot 10^{-4}$ M. + 0.1 M. HCl. 4 - 2-aminopyridine in a 4M alcoholic solution of HCl, from $5 \cdot 10^{-3}$ to $5 \cdot 10^{-5}$ M. 5 - 2-aminopyridine in concentrated H_2SO_4 (17.5M), from $3 \cdot 10^{-2}$ M to $4.5 \cdot 10^{-5}$ M. 6 - 2-aminopyridine in 72% (12 M) $HClO_4$, from $2 \cdot 10^{-3}$ to $2 \cdot 10^{-5}$ M. 7 - 1-methyl-2-aminopyridinium hydroiodide (Goldfarb). 8-pyridine in concentrated H_2SO_4. 9 - 2-aminopyridine in neutral alcohol.

"ortho band" in the far ultraviolet becomes 20 times weaker, the latter being manifested on the curve as a bend due to the superposition upon it of the stronger pyridine absorption band. The figures on the band maxima of 2-aminopyridine in chloric, sulfuric, and hydrochloric acids are listed in Table 6.

Hence, the more highly concentrated H_2SO_4 (17.5M) further weakens the "ortho absorption band" of 2-aminopyridine. The appearance of the band corresponding to pyridine is occasioned by the passing of many 2-aminopyridine molecules into the salt, again at the amino group. The influence of the NH_2 group on the pyridine ring is not completely suppressed, however, in contrast to what happens with 4-aminopyridine.

We can calculate from the band maximum of 2-aminopyridine in the middle ultraviolet (Fig. 4, Curves 5 and 4) that only some 50% of the molecules of 2-aminopyridine changes into doubly charged cations. Diluting the solution of 2-aminopyridine in sulfuric acid with 5 times its weight in water and investigating the resulting solution (15% H_2SO_4) yielded a spectral curve that precisely repeated the curve for the same compound in 15% HCl. This curve is not reproduced for the sake of brevity. Hence, the dissolution of 2-aminopyridine in concentrated H_2SO_4 involves no other processes than salt formation. We still do not know whether the formation of an intramolecular hydrogen bond or other factors prevent the complete conversion of the 2-aminopyridine into doubly charged cations; this requires further research.

SUMMARY

1. 2-Aminopyridine and 4-aminopyridine have been synthesized and their ultraviolet absorption spectra in hexane, water, alcohol, glycol, dichloroethane, and chloroform, as well as in HCl of different concentrations, in chloric acid, in concentrated H_2SO_4, and in solutions of $NaOC_2H_5$, have been investigated.

2. It has been found that the spectra of 4-aminopyridine in hexane and in dichloroethane resembles the spectra of aniline and pyridine in hexane, and the hypothesis is advanced that the aniline and pyridine bands may be due to intermolecular association of the molecules.

3. In water, glycol, alcohol, and HCl, added in percentages ranging from 0.001% to 15%, the 2- and 4-aminopyridines behave like bases, the ring nitrogen giving up a "noncovalent" electron pair to the molecule of the solvent, so that a singly charged cation may be produced. The latter is partly detected in the appearance of "para" or "ortho" types of absorption bands in the spectra, similar to what occurs with nitroaniline, hydroxybenzaldehyde, and other compounds.

4. Salt formation by 2- and 4-aminopyridines in 72% $HClO_4$ (12 M) involves the partial addition of a proton to the NH_2 group and the suppression of the influence of that group upon the ring.

5. The salt formation by 4-aminopyridine in concentrated H_2SO_4 (17.5M) is characterized by a return to the spectrum of pyridine in concentrated H_2SO_4 and, hence, by the formation of a doubly charged cation, in contrast to 2-aminopyridine in concentrated H_2SO_4, which retains, though in a greatly modified form, the spectrum corresponding to an "ortho absorption band."

6. The varying action of small percentages of water in the hexane solution upon 2-aminopyridine has been shown.

7. The "ortho" and "para" bands of the 2- and 4-aminopyridines have been found to lose intensity in solutions of sodium alcholate (an alkaline medium), which is apparently due to the elimination of the influence of the alcohol proper as a solvent.

8. No tautomerism has been found in the absorption spectra of the isomeric 2- and 4-aminopyridines.

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THE DERIVATIVES OF 8-HYDROXYQUINOLINE AND THEIR ANTIBACTERIAL ACTION

I. 8-ARYLOXY- AND 8-ALKOXY QUINOLINES

M. H. Shchukina and N. V. Savitskaya

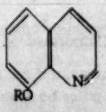
8-Hydroxyquinoline, first synthesized in 1869 by the Russian chemist N. N. Lyubavin [1], long ago attracted the attention of researchers because of its antiseptic and disinfecting action [2]. Preparation of 8-hydroxyquinoline and its derivatives, such as chinosol (8-hydroxyquinoline sulfate), and yatren [3] (the sodium salt of 7-iodo-8-hydroxyquinolyl-5-sulfonic acid mixed with sodium bicarbonate), are now used in medicine as antiseptics and in the cure of amebic dysentery and other diseases.

8-Hydroxyquinoline possesses several chemical features related to its structure, which make possible a complex tautomerism and the formation of coordination compounds, wherein it differs from the other isomeric hydroxyquinolines, which do not exhibit any antibacterial action either.

In 1944 several authors [1] put forward a hypothesis to explain the antibacterial and fungistatic action of 8-hydroxyquinoline by its combining with traces of metals that are vital to the metabolism of bacteria and fungi, forming complex salts as shown in Diagram (A), where Me is a divalent metal.

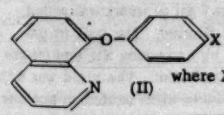
In comformity with this explanation for the antibacterial activity of 8-hydroxyquinoline and its derivatives, Albert, Rubbo, and their coauthors found that 8-methoxyquinoline and the quaternary base N-methyl-8-hydroxyquinoline, which do not form complexes with metals, are also inactive with respect to microorganisms. We were therefore interested in synthesizing a series of derivatives of 8-hydroxyquinoline with substituents either on the 8-hydroxy group or on the nitrogen and hence incapable of forming coordination compounds, so as to investigate their antibacterial activity.

The first of these compounds we looked into were the 8-alkoxy-(I) and 8-phenoxy-(II) derivatives of quinoline:



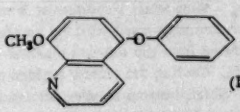
where R = C_3H_7; iso-C_3H_7; C_4H_9; iso-C_5H_{11}; C_6H_{13}; C_7H_{15}; C_8H_{17}; C_9H_{19}; $C_{10}H_{21}$; $C_{11}H_{23}$; $C_{12}H_{25}$.

(I)

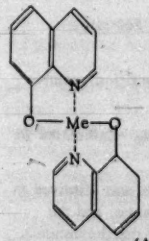


where X = H; NH_2; $NHCOCH_3$; OH

(II)



(III)



(A)

We prepared 8-phenoxyquinoline by condensing the potassium salt of 8-hydroxyquinoline with bromobenzene in the presence of copper bronze. As we know, the introduction at the para position of such substituents as the hydroxy and amino groups usually increases the antibacterial activity of compounds [5]. We therefore also synthesized 8-(p-aminophenoxy)-quinoline and 8-(p-hydroxyphenoxy)-quinoline. The initial substance was 8-(p-nitro-phenoxy)-quinoline [6], which we reduced to 8-(p-aminophenoxy)-quinoline with iron powder in aqueous alcohol, with a small quantity of hydrochloric acid present, or by hydrogen in the presence of a pyrophoric nickel catalyst. We noticed that catalytic hydrogenation, even though it slowed down very much after 3 molecules of hydrogen had been absorbed per molecule of 8-hydroxyquinoline, continued until 8-(p-aminophenoxy)-tetrahydroquinoline had been produced, which we recovered and identified as its diacetyl derivative. We synthesized 8-(p-hydroxyphenoxy)-quinoline by diazotizing 8-(p-aminophenoxy)-quinoline and decomposing the diazo compound

by boiling it with a 75% aqueous solution of sulfuric acid.

To find out how the antibacterial activity of a phenoxyquinoline changes when another simple ester group is introduced into it, we synthesized 5-phenoxy-8-methoxyquinoline (III).

8-Butoxyquinoline proved least toxic in tests on mice of all the preparations we synthesized, while possessing definite bacteriostatic action on the tuberculosis bacillus. We therefore synthesized a few of its derivatives: 5-nitro-8-butoxyquinoline, 5-acetamino-8-butoxyquinoline, and 5,7-dibromo-8-butoxyquinoline.

As we know, introducing halogen atoms into the 8-hydroxyquinoline molecule lowers the toxicity of the compounds [7]. We therefore synthesized the dichloro and dibromo derivatives of one of the most active esters: 8-octoxyquinoline.

In all the preparations we synthesized, the hydrogen in the hydroxyl group was replaced by an alkyl or phenyl group, so that they should not have manifested any antibacterial activity according to the theory of Albert, Rubbo, et al. An investigation of the antibacterial activity of these preparations and of their action on some oxidizing ferments (indophenoloxidase), carried out in the Division of Chemotherapy of the All-Union Research Institute of Pharmaceutical Chemistry under the direction of G. N. Pershin, demonstrated their activity, however. These findings led us to conclude that the antibacterial activity of 8-hydroxyquinoline and of its derivatives cannot be ascribed to one property alone: their ability to form complexes with metals, but that the structure of the molecule as a whole must be taken into consideration.

EXPERIMENTAL

I. Aryloxy Quinolines

8-Phenoxyquinoline. The potassium salt of 8-hydroxyquinoline, prepared by fusing 12.4 g (0.085 mole) of 8-hydroxyquinoline with 4.75 g (0.085 mole) of potassium hydroxide, was mixed with 1 g of copper bronze and 9.4 g (0.06 mole) of bromobenzene. The mixture was heated to 190-200° on an oil bath for 3 hours with constant stirring. After the reaction was over, the melt was poured into water, the insoluble residue being filtered out, washed with water, and extracted with alcohol. After part of the alcohol had been driven off in vacuo, we secured a dark crystalline powder, which was sublimated in vacuo and recrystallized from alcohol. B.p. 195° at 0.6 mm. A white crystalline powder (needles) with an m.p. of 104-105°, soluble in alcohol, acetone, benzene, and chloroform.

3.597 mg substance: 10.73 mg CO_2; 1.628 mg H_2O. 6.668 mg substance: 0.365 ml N_2 (20.5°, 728.5 mm). Found %: C 81.60; H 5.06; N 6.1. $C_{15}H_{11}ON$. Calculated %: C 81.45; H 5.02; N 6.33.

Picrate of 8-phenoxyquinoline: lustrous needles with an m.p. of 139-140 (from alcohol), freely soluble in acetone.

4.960 mg substance: 4.36 ml 0.01 N H_2SO_4. Found %: N 12.31. $C_{15}H_{11}ON \cdot C_6H_3O_7N_3$. Calculated %: N 12.44.

8-(p-Aminophenoxy)-quinoline. 7 ml of water and 16 g of iron powder were added to a solution of 8.3 g (0.31 mole) of 8-(p-nitrophenoxy)-quinoline in 60 ml of alcohol. The mixture was heated to the boiling point on a water bath and stirred for 2 hours while a solution of 1 ml of concentrated hydrochloric acid in 7 ml of water was added, after which the reaction mass was boiled for another 2 hours, alkalinized with soda, and filtered. The bulk of the amine was precipitated from the solution together with the hydrated iron and recovered by extracting the precipitate with alcohol (5.4 g). Cooling the filtrate yielded another gram of 8-(p-aminophenoxy)-quinoline. The yield was 87% of the theoretical. Small lustrous needles with an m.p. of 200-200.5° (from alcohol), soluble when heated in acetone and benzene, and slightly soluble in diethyl and petroleum ethers.

4.450 mg substance: 12.474 mg CO_2; 1.991 mg H_2O. 5.705 mg substance: 0.594 ml N_2 (22°, 740 mm). Found %: C 76.45; H 5.01; N 11.73. $C_{15}H_{12}ON_2$. Calculated %: C 76.77; H 5.12; N 11.86.

Picrate of the 8-quinoline-p-aminophenyl ester: needles with an m.p. of 209° (with decomposition), soluble in hot water.

4.235 mg substance: 0.626 ml N_2 (26°, 724.5 mm). Found %: N 16.08. $C_{15}H_{12}ON_2 \cdot C_6H_3O_7N_3$. Calculated %: N 16.13.

8-(p-Acetaminophenoxy)-quinoline. 0.5 gram (0.018 mole) of 8-(p-aminophenoxy)-quinoline was dissolved in 3 ml of glacial acetic acid and boiled for 8 hours. Then the excess acetic acid was driven off in vacuo, and the residual oily substance triturated with petroleum ether. This yielded 0.5 g of the substance (85% of the theoretical). A white crystalline powder with an m.p. of 169.5-171° (from alcohol), freely soluble in alcohol and acetone, less so in benzene, and insoluble in diethyl and petroleum ethers.

3.399 mg substance: 9.158 mg CO_2; 1.554 mg H_2O. 6.483 mg substance: 4.79 ml 0.01 N. H_2SO_4. Found %: C 73.48; H 5.11; N 10.34. $C_{17}H_{14}O_2N_2$. Calculated %: C 73.35; H 5.07; N 10.07.

8-(p-Aminophenoxy)-quinoline. A solution of 0.5 g of 8-(p-nitrophenoxy)-quinoline in alcohol was hydrogenated at room temperature with a pyrophoric nickel catalyst. After the amount of hydrogen required to reduce the nitro group had been absorbed (125 ml), hydrogenation was stopped, and the solution was filtered and evaporated in vacuo. The residue had an m.p. of 198-200° after recrystallization from alcohol; its mixed melting point with an 8-(p-aminophenoxy)-quinoline synthesized by another method exhibited no depression. The yield was 0.355 g (80% of the theoretical).

8-p-(Aminophenoxy)-tetrahydroquinoline. A solution of 2.8 g of 8-(p-nitrophenoxy)-quinoline in 150 ml of alcohol was hydrogenated at room temperature with 3 g of pyrophoric nickel catalyst until no more hydrogen was absorbed, the process taking 3 days. The absorbed hydrogen totaled 1250 ml. After hydrogenation was complete, the solution was filtered, and the alcohol driven off in vacuo. The substance was refined by converting it into a hydrochloride by dissolving it in the minimum quantity of alcohol and adding three times the calculated quantity of concentrated hydrochloric acid. This threw down a crystalline powder which was recrystallized from alcohol and then reconverted into the base by treating it with a soda solution. The oily substance that settled out crystallized when it was rubbed with petroleum ether. The 8-(p-aminophenoxy)-tetrahydroquinoline was a white crystalline powder (needles) with an m.p. of 68.5-70°, freely soluble in alcohol, acetone, and benzene and insoluble in petroleum ether.

3.441 mg substance: 9.230 mg CO_2; 1.999 mg H_2O. 4.962 mg substance: 0.510 ml N_2 (19.5°, 736.5 mm). Found %: C 75.34; H 6.69; N 11.63. $C_{18}H_{16}ON_2$. Calculated %: C 74.96; H 6.71; N 11.66.

8-(p-Aminophenoxy)-tetrahydroquinoline hydrochloride, was a white crystalline powder (needles) with an m.p. of 222° (with decomposition), freely soluble in cold water and when heated in alcohol or acetone.

0.2093 g substance: 13.33 ml 0.1 N. $AgNO_3$. Found %: Cl 22.58. $C_{17}H_{16}ON_2 \cdot 2HCl$. Calculated %: Cl 22.33.

8-(p-Acetaminophenoxy)-N-acetyltetrahydroquinoline. A mixture consisting of 1 g of 8-p-aminophenoxy)-tetrahydroquinoline hydrochloride, 3 ml of acetic anhydride, 3 ml of acetic acid, and 0.7 g of sodium acetate, was heated on a water bath for 3 hours. Then the reaction mass was poured into ice water, the oily substance that separated out being extracted with ether. The oily residue left after the ether had been driven off crystallized when left to stand in a vacuum desiccator for a long time. After recrystallization from a benzene-petroleum ether mixture, the 8-(p-acetaminophenoxy)-tetrahydroquinoline was a white crystalline powder with an m.p. of 125-126°, freely soluble in alcohol, ether, benzene, and acetone and slightly soluble in petroleum ether.

5.085 mg substance: 0.402 ml N_2 (25.5°, 725 mm). Found %: N 8.62. $C_{19}H_{20}O_2N_2$. Calculated %: N 8.58.

8-(p-Hydroxyphenoxy)-quinoline. 0.16 g of sodium nitrite, dissolved in 1.5 ml of water, was gradually added at 0 to +3° to a solution of 0.5 g of 8-(p-aminophenoxy)-quinoline in 10 ml of 4.5% of sulfuric acid chilled to 0°. After diazotization was complete, the solution was poured portionwise into 17 ml of boiling 75% sulfuric acid. Upon decomposition, the reaction mass was poured over ice; a small quantity of tar appeared in the form of flocs, which were filtered out. The brown precipitate thrown down when the filtrate was alkalinized with aqueous ammonia was recrystallized from a large quantity of water. After recrystallization from a mixture of alcohol and acetone, the 8-(p-hydroxyphenoxy)-quinoline was a cream-colored crystalline powder with an m.p. of 240.5-242°, freely soluble when heated in alcohol, less so in acetone and insoluble in ether.

4.090 mg substance: 11.402 mg CO_2; 1.73 mg H_2O. 6.426 mg substance: 0.332 ml N_2 (18°, 731.5 mm). Found %: C 76.03; H 4.73; N 5.83. $C_{15}H_{11}O_2N$. Calculated %: C 75.92; H 4.63; N 5.90.

5-Phenoxy-8-methoxyquinoline. 4.8 g (0.019 mole) of 5-bromo-8-methoxyquinoline was mixed in phenol with 0.8 g of copper bronze and a phenolate prepared from 4 g (0.038 mole) of phenol and 1.1 g (0.019 mole) of potassium hydroxide. The mixture was stirred as it was heated on a 180-190° oil bath for 2.5 hours. Then the melt was poured into a 5% alkali solution, the separating oily substance being removed, washed with water and dissolved in hydrochloric acid. The hydrochloric acid solution was extracted with ether, heated with charcoal, filtered, and alkalinized with aqueous ammonia. The oily liquid that separated out was extracted with ether. The residue left after the ether extraction was a dark-yellow powder (1.5 g), which colored a flame green, was insoluble in the ordinary neutral organic solvents, though soluble in concentrated hydrochloric acid, and consisted of a copper coordination compound of hydroxyquinoline. After the ether had been driven out of the ether solution, we secured 1.4 g of 5-phenoxy-8-methoxyquinoline, which was a yellow crystalline powder (needles) with an m.p. of 108-109° after two recrystallizations from petroleum ether, which was freely soluble in alcohol, acetone, ether, and benzene.

4.330 mg substance: 12.166 mg CO_2; 2.008 mg H_2O. 8.309 mg substance: 0.415 ml N_2 (23°, 741 mm). Found %: C 76.63; H 5.19; N 5.61. $C_{16}H_{13}O_2N$. Calculated %: C 76.46; H 5.22; N 5.58.

5-Phenoxy-8-methoxyquinoline picrate: yellow needles with an m.p. of 165-167° (from alcohol).

5.747 mg substance: 4.79 ml 0.01 N H_2SO_4. Found %: N 11.67. $C_{16}H_{13}O_2N \cdot C_6H_3O_7N_3$. Calculated %: N 11.66.

II. 8-Alkoxy Quinolines

We prepared the 8-alkoxy quinolines by boiling 8-hydroxyquinoline with alkyl bromides for a few hours in an alcoholic solution of potassium hydroxide. By way of example, we shall cite the synthesis of 8-propoxyquinoline. With the exception of 8-isopropoxyquinoline and 8-butoxyquinoline, which were isolated as white crystalline powders, all the esters were colorless or slightly yellowish liquids that were freely soluble in the ordinary organic solvents. The esters were identified as their picrates or hydrochlorides. In most instances the picrates of the 8-alkoxy quinolines were readily crystallizable substances, soluble in alcohol, acetone, and ethyl acetate. The constants, analyses, and yields of the synthesized 8-alkoxy quinolines are listed in the table.

8-Alkoxy Quinolines

Name of Substance		Melting point	Boiling point	Calculated %			Found %			Yield, % theory
				C	H	N	C	H	N	
8-Isopropoxyquinoline	Base	41-43°	116° at 1.4 mm	76.96	7.00	7.48	77.07	7.07	7.56	59.5
	Hydrochloride*	185-185.5 with decomp.								
8-Butoxyquinoline	Base	48-49	170-172 at 12 mm	77.56	7.52	6.36	77.91	7.66	6.91	53
	Picrate	154-155.5				13.02			12.88	
8-Isoamoxyquinoline	Base		133-134 at 0.6 mm	78.10	7.97	6.51	77.85	8.08	6.29	65
	Picrate	169-170				12.61			12.46	
8-Hexoxyquinoline	Base		150-152 at 1 mm	78.55	8.36	6.11	78.27	8.46	5.89	69
	Picrate	129-130.5				12.22			12.20	
8-Heptoxyquinoline	Base		150-152 at 0.6 mm	78.96	8.71	5.76	78.95	8.89	5.94	67
	Picrate	119-120				11.86			11.62	
8-Octoxyquinoline	Base		163-164 at 0.8 mm	79.32	9.08	5.44	79.16	9.08	5.65	66
	Picrate	101-102				11.52			11.29	
8-Nonoxyquinoline	Base		180-181 at 1 mm	79.64	9.29	5.16	79.78	9.51	5.26	54
	Picrate	101-103				11.19			11.17	
8-Decoxyquinoline	Base		175-177 at 0.5 mm	79.94	9.54	4.91	80.25	9.54	4.76	49
	Picrate	92-93.5				10.89			10.81	
8-Undecoxyquinoline	Base		170-171 at 0.5 mm	80.21	9.77	4.68	80.32	9.58	4.92	57.5
	Picrate	87-88				10.60			10.69	
8-Dodecoxyquinoline	Base		176-178 at 0.4 mm	80.45	9.98	4.47	80.87	9.94	4.28	
	Picrate	76-78				10.33			10.75	

* Found %: Cl 15.74; Calculated %: Cl 15.85.

14.5 g (0.1 mole) of 8-hydroxyquinoline and 12.3 g (0.1 mole) of propyl bromide were added to a solution of 5.6 g (0.1 mole) of potassium hydroxide in 60 ml of alcohol, and the mixture was boiled for 5 hours. Then the alcohol was driven out of the solution in vacuo, water was added to the residue, and the oily substance that separated out was extracted with ether and distilled in vacuo. This yielded 11.4 g (61% of the theoretical) of 8-propoxyquinoline as a colorless oily substance with a b.p. of 159-160° at 12 mm. The substance darkened in storage.

7.719 mg substance: 21.674 mg CO_2; 4.958 mg H_2O. 7.220 mg substance: 0.465 ml N_2 (19.5°, 749 mm). Found %: C 76.58; H 7.18; N 7.42. $C_{12}H_{15}ON$. Calculated %: C 76.96; H 7.00; N 7.48.

8-Propoxyquinoline hydrochloride, prepared by adding a concentrated alcoholic solution of hydrogen chloride to an alcoholic solution of the base, consisted of lustrous yellow needles with an m.p. of 193-194° (with decomposition), freely soluble in alcohol, water, and acetone.

4.570 mg substance: 2.845 mg AgCl. Found %: Cl 17.40. $C_{13}H_{22}ON \cdot HCl$. Calculated %: Cl 17.85.

5-Nitro-8-butoxyquinoline. 3 grams (0.0149 mole) of 8-butoxyquinoline was dissolved in 9 ml of nitric acid (d = 1.5), and the solution was heated for 3 hours on a water bath at 70°. Then the reaction mass was poured into ice water, neutralized with soda, the precipitated crystals being filtered out and washed with water. This yielded 3 g of 5-nitro-8-butoxyquinoline (81.7% of the theoretical). Yellow needles with an m.p. of 107-108.5° (from alcohol), soluble in acetone, diethyl ether, and petroleum ether.

3.406 mg substance: 7.909 mg CO_2; 1.719 mg H_2O. 4.208 mg substance: 0.419 ml N_2 (17.5°, 742 mm). Found %: C 63.33; H 5.65; N 11.42. $C_{13}H_{16}O_3N_2$. Calculated %: C 63.39; H 5.73; N 11.38.

5-Acetamino-8-butoxyquinoline. A mixture consisting of 1.2 g (0.0047 mole) of 5-nitro-8-butoxy-quinoline, 8.5 ml of alcohol, 2.5 ml of water, and 2.5 g of iron powder was boiled for 2 hours while a solution of 0.15 ml of concentrated hydrochloric acid in 1 ml of water was gradually added, with constant stirring. After two hours of heating, the hot reaction mass was alkalinized with soda and filtered, the filtrate being extracted with ether. Then the ether was driven off, and the strongly tarred substance that settled out was converted into the hydrochloride by dissolving it in a saturated alcoholic solution of hydrogen chloride. The 5-amino-8-butoxyquinoline hydrochloride that crystallized out as the solution cooled was recrystallized several times from alcohol, which yielded a white crystalline powder that darkened quickly when exposed to the air.

One gram of 5-amino-8-butoxyquinoline was mixed with 3 ml of acetic anhydride, 1.5 ml of glacial acetic acid, and 0.3 g of anhydrous sodium acetate, and the mixture was heated on a boiling water bath for 3 hours. After decomposition of the excess acetic anhydride, the reaction mass was poured into ice water, the crystals produced being filtered out and recrystallized from 2-% aqueous alcohol.

5-Acetamino-8-butoxyquinoline is a white crystalline powder with an m.p. of 171-172°, freely soluble in the usual organic solvents.

4.211 mg substance: 10.822 mg CO_2; 2.609 mg H_2O. 4.647 mg substance: 0.451 ml N_2 (20°, 728.5 mm). Found %: C 70.08; H 6.93; N 10.85. $C_{13}H_{18}O_2N_2$. Calculated %: C 70.00; H 6.67; N 10.89.

5,7-Dibromo-8-butoxyquinoline. 8.7 grams (0.024 mole) of 5,7-dibromo-8-hydroxyquinoline and 4 g (0.029 mole) of butyl bromide were added to a solution of 1.35 g (0.024 mole) of potassium hydroxide in 80 ml of alcohol, and the mixture was boiled for 6 hours. Then the alcohol was driven off in vacuo, the reaction mass was poured into water, and the oily substance that separated out was extracted with ether. After the ether had been driven off, the 5,7-dibromo-8-butoxyquinoline was recrystallized twice from alcohol. A white crystalline powder with an m.p. of 61.5-63°, freely soluble in ether and acetone and less so in alcohol.

5.580 mg substance: 5.940 mg AgBr. 7.817 mg substance: 0.274 ml N_2 (17.5°, 729.3 mm). Found %: Br 45.29; N 3.95. $C_{13}H_{15}ONBr_2$. Calculated %: Br 44.53; N 3.90.

5,7-Dichloro-8-octoxyquinoline. 3.6 grams (0.017 mole) of 5,7-dichloro-8-hydroxyquinoline and 4 g (0.0207 mole) of octyl bromide were added to a solution of 0.95 g (0.017 mole) of 5,7-dichloro-8-hydroxyquinoline in 50 ml of methanol, and the mixture was boiled for 20 hours. The alcohol was then driven off in vacuo, and the reaction mass was diluted with water and extracted with ether, the ether solution being dried with potash. Then the ether was driven off, and the residue recrystallized from methanol. The yield was 2.8 g (51% of the theoretical). A white crystalline powder with an m.p. of 41.5-43°, freely soluble in alcohol, ether, acetone and chloroform.

2.860 mg substance: 2.534 mg AgCl. 7.605 mg substance: 0.297 ml N_2 (20.5°, 713 mm). Found %: Cl 21.91; N. 4.26. $C_{17}H_{21}ONCl_2$. Calculated %: Cl 21.74; N 4.29.

5,7-Dibromo-8-octoxyquinoline. A mixture consisting of 10.1 g (0.033 mole) of 5,7-dibromo-8-hydroxy-quinoline, 9 g (0.047 mole) of octyl bromide, and 1.85 g (0.033 mole) of potassium hydroxide in 90 ml of alcohol was heated on a boiling water bath for 10 hours. The alcohol was then driven off in vacuo, and the reaction mass was diluted with water and extracted with ether, the ether solution being dried with potash. Driving off the ether in vacuo and recrystallizing the residue from methanol yielded 7.5 g (54% of the theoretical) of 5,7-dibromo-8-octoxyquinoline. A white crystalline powder (needles), freely soluble in alcohol, ether, acetone, chloroform, and ethyl acetate.

6.718 mg substance: 1.62 ml 0.01 N. H_2SO_4. 3.420 mg substance: 3.130 mg AgBr. Found %: N 3.38; Br 38.95. $C_{17}H_{21}ONBr_2$. Calculated %: N 3.37; Br 38.53.

SUMMARY

The following have been synthesized: 1) 8-phenoxyquinoline, its p-amino, p-acetoamino, and p-hydroxy derivatives, and 5-phenoxy-8-methoxyquinoline;

2) A series of alkoxy quinolines with C_3–C_{12} alkyl groups, the normal ones and some branched ones;

3) 5-nitro-8-butoxyquinoline, 5-acetamino-8-butoxyquinoline, 5,7-dibromo-8-butoxyquinoline, 5,7-dichloro-8-octoxyquinoline, and 5,7-dibromo-8-octoxyquinoline.

These compounds possess definite antibacterial and antiferment activity, notwithstanding the absence of a free hydroxyl group at the 8 position and their resultant inability to form complexes with metals. This leads us to conclude that the explanation proposed by Albert and Rubbo for the antibacterial activity of 8-hydroxyquinoline is inadequate.

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THE DERIVATIVES OF 8-HYDROXYQUINOLINE AND THEIR ANTIBACTERIAL ACTION

II. THE N-OXIDES OF 8-HYDROXYQUINOLINE AND ITS ETHERS

M. N. Shchukina and N. V. Savitskaya

Not much research has been done on the N-oxides of the hydroxyquinolines and their derivatives [1]. The present paper describes the synthesis and properties of the N-oxides of 8-hydroxyquinoline and of some of the latter's derivatives, which are of interest in antibacterial research.

As we noted in the preceding paper, the antibacterial activity of 8-hydroxyquinoline has been attributed to its ability to form complexes with metals that are vitally needed by bacteria. If this were so, it might be expected that the N-oxides of 8-alkoxyquinolines would have no antibacterial activity. The N-oxide of 8-hydroxyquinoline and the N-oxides of several of its ethers which we have synthesized, exhibit distinct antibacterial activity, however, as has been established by research carried out in the Division of Chemotherapy of the All-Union Research Institute of Pharmaceutical Chemistry under the direction of G. N. Pershin. This confirmed our conclusion that the antibacterial activity of 8-hydroxyquinoline and of its derivatives cannot be ascribed to only one of the properties of these compounds – their ability to form coordination compounds, the structure of the molecule as a whole having to be taken into account.

Two methods were employed in synthesizing the N-oxides of 8-hydroxyquinoline and of its ethers: oxidation with perbenzoic acid in chloroform solution, and oxidation with hydrogen peroxide in glacial acetic acid. The reactions are not identical in the two cases, as might have been expected, when we consider the effect of the solvent upon the equilibrium between the tautomeric forms of 8-hydroxyquinoline, which depends largely upon the nature of the solvent, say, its dielectric constant and the pH of the medium.

We were unable to oxidize the 8-alkoxy quinolines to the respective N-oxides by means of hydrogen peroxide in glacial acetic acid. When 8-hydroxyquinoline was reacted with a large excess (6 moles) of 25% hydrogen peroxide in glacial acetic acid, a small amount (5-7%) of the N-oxide of 8-hydroxyquinoline was produced, plus a large quantity of acidic substances that were dark in color and high-melting. We did not find any of the well-known and readily isolated aromatic or pyridine acids. This leads us to conclude that when 8-hydroxyquinoline is oxidized under these conditions, the formation of the N-oxide is paralleled by the rupture of the ring bonds and intermolecular condensation. This might have been expected in the light of the activity of the hydrogen atoms at the 5 and 7 positions.

Oxidation of 8-hydroxyquinoline and of its ethers by perbenzoic acid at room temperature produced yields ranging between 12% and 40%. Part of the substances tarred, while another part did not enter into the reaction. The N-oxides produced by oxidation were isolated as their picrates, which were then converted into hydrochlorides and purified.

The N-oxides of 8-hydroxyquinoline and of its ethers are rather stable compounds. More specifically, they do not liberate iodine from a potassium iodide solution even after prolonged boiling, though several authors consider this reaction to be typical of the N-oxides [2]. They are not reduced by sulfuric anhydride even when heated with it, as has been observed for many other N-oxides [3], nor by zinc dust in acetic or dilute sulfuric acid [4]. The N-oxides of the 8-alkoxy quinolines can be reduced only by sodium hydrosulfite in a water-alcohol medium [5]. The N-oxide of 8-hydroxyquinoline is reduced to 8-hydroxyquinoline catalytically with a pyrophoric nickel catalyst.

EXPERIMENTAL

N-Oxide of 8-Hydroxyquinoline. A solution of 4.5 g (0.036 mole) of 8-hydroxyquinoline in 20 ml of chloroform was poured during the course of 20 minutes into a chloroform solution (90 ml) of perbenzoic acid chilled to +1° and containing 0.512 g (0.032 equiv.) of active oxygen according to titration. Then the temperature was raised during the course of 5 hours to room temperature, and the mixture was set aside to stand overnight. The next day

the chloroform was driven off in vacuo, and the remaining tacky mass was washed by decantation, first with concentrated aqueous ammonia and then with water. The N-oxide of 8-hydroxyquinoline remained at the bottom of the vessel as an oily liquid, the flocculent crystalline 8-hydroxyquinoline floating on top and being easily removable. The N-oxide of 8-hydroxyquinoline crystallized when rubbed with ether. The product consisted of yellow needles with an m.p. of 138-139.5° after two recrystallizations from water. Freely soluble when heated in ordinary organic solvents.

3.255 mg substance: 7.970 mg CO_2; 1.241 mg H_2O. 7.570 mg substance: 0.566 ml N_2 (18.5°, 742 mm). Found %: C 67.40; H 4.31; N 8.55. $C_9H_7O_2N$. Calculated %: C 67.06; H 4.38; N 8.69.

Catalytic reduction of 8-hydroxyquinoline N-oxide. A solution of 0.5 g of 8-hydroxyquinoline N-oxide in alcohol was hydrogenated at room temperature for 3.5 hours with a pyrophoric nickel catalyst, 80 ml of hydrogen being absorbed (70 ml being called for theoretically). After the alcohol had been driven off in vacuo, the residue was filtered out and treated with hot alcohol. When the alcoholic solution was chilled, a white crystalline substance with an m.p. of 69-72° settled out, which exhibited no depression when mixed with 8-hydroxyquinoline. The alcohol-insoluble substance was a yellow-green crystalline powder that decomposed without melting when heated above 250°, was insoluble in alcohol, ether, acetone, or benzene, was soluble in xylene, and was a coordination nickel compound of hydroxyquinoline. This compound was boiled with concentrated hydrochloric acid, the solution being evaporated to dryness and extracted with alcohol; driving off the solvent and treating the residue with ammonia yielded some more 8-hydroxyquinoline.

5-Chloro-8-hydroxyquinoline N-oxide. A solution of 5.3 g (0.029 mole) of 5-chloro-8-hydroxyquinoline in 90 ml of chloroform was added to a chloroform solution (159 ml) of perbenzoic acid, containing 0.576 g (0.076 equiv.) of active oxygen, and the mixture was set aside to stand overnight. Then an alcoholic solution of 6.6 g of picric acid was added to the darkened solution. Evaporating the alcohol-chloroform solvent in vacuo yielded a highly tarred picrate, which could not be purified by recrystallization from alcohol. The picrate was dissolved in concentrated hydrochloric acid, the precipitated picric acid being filtered out, and the hydrochloric solution being extracted with hot benzene. Then the hydrochloric solution was alkalinized with ammonia and extracted with ether. Driving off the ether yielded 0.45 g of a substance, which was recrystallized from alcohol and then from ligroin. 5-Chloro-8-quinoline N-oxide is a yellow crystalline powder with an m.p. of 169-170°, freely soluble when heated in alcohol, acetone, and ether.

5.130 mg substance: 3.799 mg AgCl. 6.755 mg substance: 0.430 ml N_2 (22°, 730 mm). Found %: Cl 18.32; N 7.21. $C_9H_6O_2NCl$. Calculated %: Cl 18.13; N 7.16.

N-Oxides of the 8-alkoxy quinolines. We cite by way of example the synthesis of the hydrochloride of 8-methoxyquinoline N-oxide. The constants, analysis, and yields of the other synthesized hydrochlorides of the N-oxides of the 8-alkoxy quinolines, and of their picrates and of some bases are given in the table.

The picrates of the N-oxides of the 8-alkoxy quinolines are crystalline substances that are freely soluble when heated in alcohol and acetone, and are insoluble in ether.

The hydrochlorides of the N-oxides of the 8-alkoxy quinolines are colorless or yellow crystalline powders (needles), that are soluble in alcohol, acetone and ethyl acetate and are insoluble in ether.

Hydrochloride of 8-methoxyquinoline N-oxide. A solution of 6.3 g (0.04 mole) of 8-methoxyquinoline in 20 ml of chloroform was added to 125 ml of a chloroform solution of perbenzoic acid containing 0.64 g (0.04 equiv.) of active oxygen by titration. The mixture was allowed to stand overnight. The next day the oxidizing property of the solution had vanished completely. An alcoholic solution of 9.4 g (0.41 mole) of picric acid was added to the reaction mass, the precipitated picrate (12.2 g with an m.p. of 125-134°) being filtered out and twice recrystallized from alcohol. Then the picrate was treated with 30 ml of concentrated hydrochloric acid, the picric acid being filtered out, and the residue extracted repeatedly with hot benzene. The acid solution was evaporated at 30-40° in vacuo until crystallization set in, violent foaming being observed. The crystals were filtered out of the oily substance, which consisted principally of 8-methoxyquinoline hydrochloride with a trace of hydrochloride of the N-oxide and recrystallized twice from alcohol to which ether had been added until the solution turned cloudy. This yielded 3 g (35.8% of the theoretical) of the hydrochloride of 8-methoxyquinoline N-oxide. A yellow crystalline powder (needles) freely soluble in water, alcohol and acetone, insoluble in ether. It darkens when allowed to stand exposed to the light.

3.124 mg substance: 6.482 mg CO_2; 1.389 mg H_2O. 7.000 mg substance: 0.392 ml N_2 (20.5°, 745 mm). 6.625 mg substance: 4.524 mg AgCl. Found %: C 56.59; H 4.97; N 6.41; Cl 16.89. $C_{10}H_9O_3N \cdot HCl$. Calculated %: C 56.72; H 4.77; N 6.62; Cl 16.76.

The picrate of 8-methoxyquinoline N-oxide. Consisted of yellow needles with an m.p. of 133-134° (from alcohol), soluble when heated in alcohol and acetone, and insoluble in ether.

4.900 mg substance: 0.604 ml N_2 (23.5°, 733 mm). Found %: N 13.69. $C_{10}H_9O_2N \cdot C_6H_3O_7N_3$. Calculated %: N 13.86.

Reduction of the N-oxide of 8-butoxyquinoline. 0.25 gram of sodium hydrosulfite was added to a solution of 0.2 g of 8-butoxyquinoline N-oxide hydrochloride in 5 ml of alcohol and 5 ml of water, and the mixture was boiled for 1 hour. Then another 0.25 g of sodium hydrosulfite was added, and heating was continued for another 2 hours. The alcohol was driven off in vacuo, and then the reaction mass was alkalinized with ammonia and extracted with ether. An ether solution of picric acid was added to the ether extract, the resultant crystals being filtered out and recrystallized twice from an alcohol-ether mixture, m.p. 152-155°. Their mixed melting point with 8-butoxyquinoline picrate exhibited no depression. The N-oxides of 8-heptoxyquinoline and 8-decoxyquinoline were reduced similarly. The picrates precipitated after reduction exhibited no depression when mixed with the respective picrates of 8-heptoxyquinoline and 8-decoxyquinoline.

The N-Oxides of 8-Alkoxy Quinolines

Name of Substance		Melting point	Calculated C	Calculated H	Calculated N	Calculated Cl	Experimental C	Experimental H	Experimental N	Experimental Cl	% theoretical yield
8-Ethoxyquinoline N-oxide	Hydrochloride	152° with decomp	58.53	5.36	6.21	15.72	58.60	5.24	6.09	15.98	22.3
	Picrate	137 - 138			13.39				13.45		
8-Propoxyquinoline N-oxide	Hydrochloride	132 - 134	60.01	5.89	5.84	14.80	60.20	5.90	5.92	15.04	25
8-Isopropoxyquinoline N-oxide	Hydrochloride	135-136 with decomp	60.01	5.89	5.84	14.80	59.88	5.80	6.04	15.09	12
8-Butyoxyquinoline N-oxide	Hydrochloride	120 - 121.5	61.52	6.36	5.52	13.98	61.56	6.22	5.56	14.09	13.5
	Picrate	119 - 120			12.55				12.70		
8-Isoamoxyquinoline N-oxide	Hydrochloride	114 - 115.5	62.79	6.78	5.23	13.25	62.88	6.98	5.11	13.42	16
	Picrate	115 - 116			12.17				12.19		
8-Hexoxyquinoline N-oxide	Hydrochloride	107 - 108	63.92	7.15	4.92	12.59	63.58	7.37	4.97	12.72	37
	Picrate	101.5-102.5			11.81				12.00		
8-Heptoxyquinoline N-oxide	Base	45 - 46.5	74.08	8.16	5.40		73.94	8.00	5.47		
	Hydrochloride	109 - 110			4.74	11.99			4.63	12.05	41
	Picrate	88.5 - 89			11.71				11.68		
8-Octoxyquinoline N-oxide	Hydrochloride	117.5-118.5	65.88	7.81	4.52	11.44	65.98	7.80	4.38	11.54	38.6
	Picrate	98 - 99			11.15				10.99		
8-Nonoxyquinoline N-oxide	Hydrochloride	114.5-116	66.73	8.13	4.32	10.95	66.70	8.17	4.15	10.72	
	Picrate	98 - 100			10.84				10.72		
8-Decoxyquinoline N-oxide	Base *	52 - 54	71.42	9.16	4.39		71.61	9.11	4.55		
	Hydrochloride	115.5-117	67.52	8.36	4.15	10.49	67.50	8.39	4.2	10.76	42.2
	Picrate	105.5-106.5			10.56				10.47		
8-Undecoxyquinoline N-oxide	Hydrochloride	118.5-120	68.24	8.39	3.98	10.08	68.21	8.35	4.16	10.12	22.5
	Picrate	102 - 103			10.29				10.37		

* Calculated %: H_2O 5.74. Found %: H_2O 5.64.

SUMMARY

A description is given of the synthesis and properties of the N-oxides of 8-hydroxyquinoline, 5-chloro-8-hydroxyquinoline, and of the 8-alkoxy quinolines with C_1—C_{11} radicals, which possess definite antibacterial activity, notwithstanding their inability to form coordination compounds.

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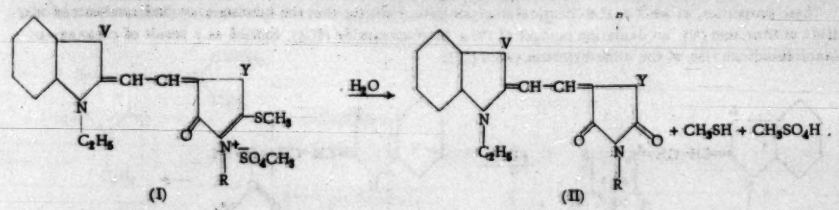
MEROCYANIN DYES THAT ARE DERIVATIVES OF RHODANINE

IV. THE STRUCTURE OF THE DECOMPOSITION PRODUCTS OF QUATERNARY SALTS OF DIMETHINE MEROCYANINS

Z. P. Sytnik, L. L. Levkoev, M. V. Deichmeister, and L. D. Zhilina

In one of our previous reports [1] we have shown that the methylmethylsulfate of 2-methylmercapto-5-(3'-ethylbenzothiazolinyliden-2'-ethylidene)-thiazolinone-(4) (I: V and Y = S, R = CH_3) is highly unstable, being hydrolyzed even when recrystallized from ethyl alcohol, precipitating methanethiol and producing a merocyanin with an N-methylthiazolidinedione-(2,4) group (II: V and Y = S; R = CH_3). It was subsequently [2] found that the decomposition of the quaternary salts of other analogous derivatives of thiazolinone-(4) and of selenazolinone-(4) and imidazolinone-(4) having the general structure of (I) proceeds along the same lines:

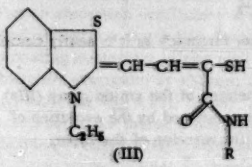


(I) (II)

V = O, S, Se, CH=CH or $C(CH_3)_2$,
Y = S, Se or NH,
R = CH_3, C_2H_5 or C_6H_5.

Hence, this process is a convenient method of synthesizing merocyanin derivatives of thiazolidinedione-(2,4) (II).

A paper by A. van Dormael was published at the end of 1949 [3], in which the instability of the quaternary salts of thiazolinone-(4) derivatives (I: Y and V = S; R = C_2H_5 or C_6H_5) in a water-alcohol medium is likewise noted. The author ascribes Structure (III) to the decomposition products of these salts, however, on the assumption that this involves the rupture of the carbonyl ring.



(III)

A. van Dormael considers the sole confirmation of this structure of the decomposition products of these salts to be the results of their chemical analysis, which he believes agree satisfactorily with the values calculated for the formula (III).

We had previously [2] secured the decomposition products of the quaternary salts described by A. van Dormael. When we compare the physical constants of these compounds with the corresponding figures cited by A. van Dormael, we find that the melting points and absorption maxima are identical or else extremely close, so that the same products were evidently secured in both instances. This makes the discrepancies in the results of chemical analysis all the more incomprehensible; in our case, these results agreed satisfactorily with the Formula (II) (V and Y = S; R = C_2H_5 or C_6H_5) for both products, whereas A. van Dormael's findings are very much at variance with Formula (II) and even with his proposed Structure (III) as far as the N-ethyl derivative is concerned.

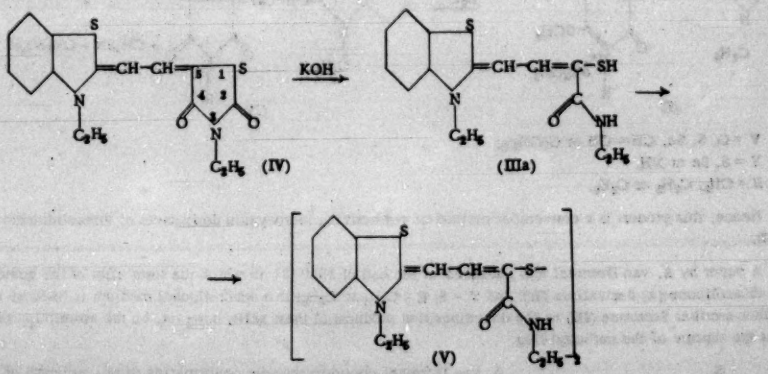
Discussing the probability of the rupture of the thiazoline ring in quaternary salts of the merocyanins when their water-alcohol solutions are heated, A. van Dormael writes: "There is nothing extraordinary about this reaction,

except the ease with which it occurs." We thought that ring cleavage was unlikely under such mild conditions, since it is known that analogous reactions take place, say, for the derivatives of benzothiazole, only when the latter are heated with concentrated caustic alkalies [4].

In special experiments we found that no carbon dioxide was evolved during the decomposition of the quaternary salt (I) (V and Y = S; R = C_2H_5) in a water-alcohol medium, though this evolution should have been expected if the carbonyl ring were ruptured, yielding a Type (III) compound; this is a convincing refutation of the reaction course advanced by A. van Dormael.

On the other hand, when the merocyanin (IV) [the decomposition product of the quaternary salt (I) when V and Y = S and R = C_2H_5] is heated with 5-7% alcoholic solution of potassium hydroxide, potassium carbonate is thrown down, and the solution turns an orange-yellow. No precipitate is thrown down when the solution is diluted with water, though the solution rapidly grows cloudy upon standing, due to oxidation by atmospheric oxygen. When air is passed through this solution or hydrogen peroxide is added to it, a dark-brown precipitate settles out. The resultant substance is very slightly soluble in water and aqueous alkalies, though fairly freely soluble in benzene alcohol, and chloroform; it dissolves readily in dilute hydrochloric acid, producing a colorless solution, from which the initial product may be recovered by neutralization. When this compound is reduced with sodium sulfite in an alkaline medium, an orange-yellow solution is produced, from which it can be reprecipitated by passing air through it or by adding hydrogen peroxide.

These properties, as well as the chemical analysis data, indicate that the substance we had synthesized was a disulfide of Structure (V), an oxidation product of the α mercaptoamide (IIIa), formed as a result of cleavage of the thiazolidinedione ring of the dimethylmerocyanin (IV):



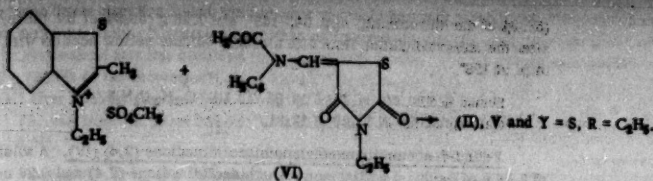
We have not yet succeeded in isolating the compound (IIIa) in the pure state, inasmuch as it is nearly completely oxidized to the disulfide (V) during the process of isolation.

Under these conditions, the principal reaction of ring cleavage, with the retention of the amido group (IIIa) is evidently paralleled by partial ring cleavage at the 1,2 and 3,4 bonds. This is demonstrated by the evolution of ethylamine during the reaction, as indicated by its characteristic odor and the alkaline reaction of the vapor.

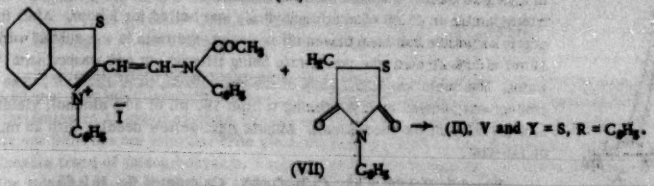
When the lemon-yellow filtrate of the disulfide (V) is alkalized, a small quantity of a light-yellow substance that is freely soluble in aqueous alkalies is precipitated. This compound may be a product of the more far-reaching disintegration of the thiazolidinedione ring. This substance is under investigation at the present time.

We synthesized two diethylmerocyanins (II: V and Y = S; R = C_2H_5 or C_6H_5) from the thiazolidinedione-(2,4) derivatives (VI and VII) in order to confirm the structure (II) we had proposed for the decomposition products of the quaternary salts of the merocyanins (I). (See top of next page).

The synthesized compounds proved to be the same as the corresponding decompositionproducts of the quaternary salts (I: V and Y = S; R = C_2H_5 or C_6H_5), judging by their melting points and the shape of their absorption curves and the location of the maximum.

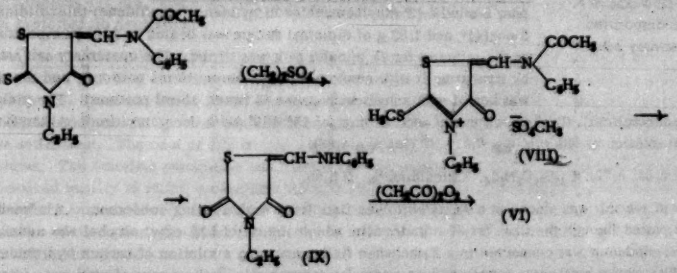


(VI)



(VII)

We synthesized 3-ethyl-5-acetanilinomethylenethiazolidinedione-(2,4) (VI) as indicated below, the procedure being also founded upon hydrolysis of the quaternary salt (VIII). The structure of the intermediate (IX) and end (VI) products was corroborated by the chemical analysis findings.



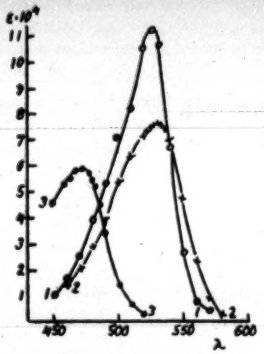
We have therefore definitely established that heating the quaternary salts (I) in an aqueous or an aqueous-alcoholic medium results in hydrolysis, yielding the merocyanins (II), and that no cleavage of the carbonyl-containing ring takes place. Hence, the reaction sequence proposed by A. van Dormael is erroneous.

It should be noted that the products described by A. van Dormael contained appreciable contaminations in many instances, which may be the reason for the false conclusions he drew from his research. Thus, A. van Dormael cites an absorption coefficient at 475 mμ for the decomposition product of the quaternary salt, in the case of the N-ethyl derivative, that is 240 times smaller than that of the pure preparation ($\log \epsilon_{475}$ 2.38 instead of 4.77). The corresponding quaternary salt he used was already largely decomposed, as indicated by the presence of a subordinate absorption maximum at 474 mμ, the intensity of which is more than 4 times that of the principal maximum ($\log \epsilon_{533}$ 3.91; $\log \epsilon_{474}$ 4.63). Lastly, A. van Dormael gives two absorption maxima, at 531 mμ and 501 mμ, of approximately the same intensity ($\log \epsilon_{531}$ 4.69; $\log \epsilon_{501}$ 4.51), for the initial merocyanin, 3-ethyl-5-(3'-ethylbenzothiazolinyliden-2'-ethylidene)-thiazolidinethion-(2)-one-(4).

Moreover, as we see from the graph, all these compounds possess only one, fairly narrow absorption band in the visible region, with extinction coefficients of the same order of magnitude.

EXPERIMENTAL

3-Ethyl-5-anilinomethylenethiazolidinedione-(2,4) (VII). 3 Grams of 3-ethyl-5-acetanilinomethylenethiazolidinethion-(2)-one-(4) and 3.78 g of dimethyl sulfate were heated together for 30 minutes to 120° (temperature within the mixture). After the mixture had cooled, the quaternary salt was washed with absolute ether (twice with 20-ml portions), the tarry residue being dissolved in 60 ml of 50% alcohol and the solution being boiled for 1 hour, methanethiol separating out. The next day the precipitate was filtered out and washed with alcohol. The yield was 1.4 g



1 - 3-ethyl-5-(3'-ethylbenzothiazolinyliden-2'-ethylidene)-thiazolidinethion-(2)-one-(4); 2 - quaternary salt (I; V and Y = S; R = C_2H_5); 3 - decomposition product of the quaternary salt (IV).

(56.4% of the theoretical), m.p. 147-148°, and 1.26 g (50.8% of the theoretical) after the recrystallization from 50% alcohol. Minute yellow needles with an m.p. of 158°.

Found %: N 11.30, 11.42; S 12.85, 13.13. $C_{12}H_{12}O_2N_2S$. Calculated %: N 11.29; S 12.91.

3-Ethyl-5-acetanilinomethylenethiazolidinedione-(2,4) (IV). A solution of 1.24 g of 3-ethyl-5-anilinomethylenethiazolidinedione-(2,4) and 0.26 ml of triethylamine in 15 ml of acetic anhydride was boiled for 1 hour. After the acetic anhydride had been driven off in vacuo, the residue was rubbed with 10 ml of 50% alcohol, the precipitate being filtered out and washed with water. The yield was 1.32 g (91% of the theoretical, m.p. 125-126°. The product was purified by crystallizing it from 180 ml of 30% alcohol, yielding 1.05 g (72.5% of the theoretical). Minute light-yellow needles with an m.p. of 115-116°.

Found %: N 9.68, 9.83. $C_{14}H_{14}O_3N_2S$. Calculated %: N 9.65.

3-Ethyl-5-(3'-ethylbenzothiazolinyliden-2'-ethylidene)-thiazolidinedione-(2,4) (II; V and Y = S; R = C_2H_5). 1. Decomposition of the quaternary salt (I) (V and Y = S; R = C_2H_5) in a water-alcohol medium). A mixture of 1.4 g of pure 3-ethyl-5-(3'-ethylbenzothiazolinyliden-2'-ethylidene)-thiazolidinethion-2-one(4)* and 1.52 g of dimethyl sulfate was heated to 130° (temperature within the mixture) for 15 minutes as it was stirred. The quaternary salt was washed by triturating it with absolute ether (4 times, 10-ml portions), and the residue was boiled with anhydrous benzene (3 times, 15-ml portions). The yield was 1.82 g (95 % of the theoretical). Dark-brown prisms with an m.p. of 188-189° (with decomposition). Absorption maximum of a methanol solution at 530 mμ ε_{530} $7.71 \cdot 10^4$ (log ε_{530} 4.88).

Found %: N 5.64, 5.75. $C_{18}H_{22}O_5N_2S_4$. Calculated %: N 5.90.

1.82 Grams of the salt was placed in a round-bottomed flask fitted with a reflux condenser. Air freed of its carbon dioxide was passed through the flask for 30 minutes after which 100 ml of 50% ethyl alcohol was added, and the upper end of the condenser was connected to a Tishchenko flask containing a solution of barium hydroxide. The outlet tube of the Tishchenko bottle was connected to a water-jet pump, and a weak current of air freed of carbon dioxide was sucked through the system. The liquid was boiled for 2 hours, the barium hydroxide solution not exhibiting any turbidity. After the solution had cooled, the precipitated deposit was filtered out and washed with alcohol and ether. The yield was 1.08 g (87.6% of the theoretical), m.p. 220-221° with decomposition. The melting point was unaffected by recrystallization from 180 ml of alcohol. Orange needles, freely soluble in alcohol, benzene and ether, insoluble in water or aqueous alkali. Absorption maximum of an alcoholic solution: 472 mμ, ε_{472} $5.89 \cdot 10^4$ (log ε_{472} 4.77).

Found %: N 8.24; S 19.44, 19.10; C 57.94, 58.05; H 5.04, 4.92. (II, V, Y = S, R = C_2H_5) $C_{16}H_{16}O_2N_2S_2$. Calculated %: N 8.42; S 19.29; C 57.80; H 4.85. (III, R = C_2H_5) $C_{15}H_{15}ON_2S_2$. Calculated %: N 9.15; S 20.91; C 58.82; H 5.89. (According to A. van Dormael: Found %: N 9.07; S 20.29; C 59.73; H 5.24).

2. From 3-ethyl-5-acetanilinomethylenethiazolidinedione-(2,4) (IV). A solution of 0.87 g of 3-ethyl-5-acetanilinomethylenethiazolidinedione-(2,4) and 1.05 g of 2-methylbenzothiazole ethyl-p-toluenesulfonate in 15 ml of pyridine was boiled for 1 hour. The precipitated dye was filtered out and washed with water and with alcohol. The yield was 0.39 g (39% of the theoretical). M.p. 219-220° (with decomposition). Absorption maximum in ethyl alcohol: 472 mμ, ε_{472} $5.89 \cdot 10^4$ (log ε_{472} 4.75). The mixed melting point of this dye with the sample secured by the first method exhibited no depression.

3-Phenyl-5-(3'-ethylbenzothiazolinyliden-2'-ethylidene)-thazolidinedione-(2,4) (II; V and Y = S; R = C_6H_5). 1. Decomposition of the quaternary salt (I) (V and Y = S; R = C_6H_5) in aqueous alcohol. A mixture of 0.79 g of 3-phenyl-5-(3'-ethylbenzothiazolinyliden-2'-ethylidene)-thiazolidinethion-(2)-one-(4) and 0.76 g of dimethyl sulfate

* M.p. 262-264° (with decomposition; absorption maximum of an alcoholic solution: 524 mμ, ε_{524} $11.31 \cdot 10^4$ (log ε_{524} 5.05).

was heated to 130° for 15 minutes. After the residue had been washed with absolute ether, it was boiled twice with anhydrous benzene (using 15-ml portions each time). The yield was 0.84 g (80% of the theoretical), m.p. 210-211° (with decomposition). Absorption maximum of an alcoholic solution: 533 mμ, ϵ_{533} $6.03 \cdot 10^4$ (log ϵ_{533} 4.78). 0.84 g of the synthesized salt was dissolved in 30 ml of 50% alcohol, and the solution was boiled for 30 minutes, yielding 0.72 g (94.5% of the theoretical), m.p. 225-227° (with decomposition). The yield totaled 0.52 g (68.4% of the theoretical) after recrystallization from 150 ml of alcohol. Bright-red prisms with an m.p. of 229-230° (with decomposition) (A. van Dormael gives 230-231°). Absorption maximum of an alcoholic solution: 476 mμ; ϵ_{476} $8.13 \cdot 10^4$ (log ϵ_{476} 4.91).

Found %: N 7.14; S 16.64, 16.57; C 63.17, 63.02; H 4.23, 4.33. (II' V, Y = S, R = C_6H_5) $C_{20}H_{16}O_2N_2S_2$. Calc. %: N 7.36; S 16.85; C 63.13; H 4.23 (III, R = C_6H_5). $C_{19}H_{16}O_2N_2S_2$. Calculated %: N 7.90; S 18.07. (According to A. van Dormael: Found %: N 7.69, 7.59; S 18.31, 18.26).

2. From 3-phenylthiazolidinedione-(2,4) and 2-(β-acetanilinovinyl)-benzothiazole (V) ethiodide. A solution of 0.63 g of 3-phenylthiazolidinedione-(2,4), 1.38 g of 2-(β-acetanilinovinyl)-benzothiazole ethiodide, and 0.42 g of triethylamine in 15 ml of absolute alcohol was heated for 30 minutes on a boiling water bath. The dye began to settle out from the hot solution. The yield was 0.85 g (74.5% of the theoretical), m.p. 190-194°. To remove the noticeable trace of thiacarbocyanin, a solution of the dye in benzene was drawn through a tube filled with alumina. As the solution passed through the layer of alumina, two layers were formed: a top red-violet (carbocyanin) layer, and a bottom orange-yellow (merocyanin) layer. The latter was washed out with benzene, the carbocyanin remaining on the alumina. The benzene solution was evaporated, the residue being crystallized from ethyl alcohol. The yield was 0.42 g (37.8% of the theoretical). Bright-red needles with an m.p. of 229-230°. Absorption maximum of an alcoholic solution: 476 mμ, ϵ_{476} $8.05 \cdot 10^4$. The mixed melting point of this dye and a sample produced by the first method exhibited no depression.

Action of alcoholic alkali on 3-ethyl-5-(3'-ethylbenzothiazolinyliden-2'-ethylidene)-thiazolidinedione-(2,4). To a suspension of 1.32 g of 3-ethyl-5-(3'-ethylbenzothiazolinyliden-2'-ethylidene)-thiazolidinedione-(2,4)* in 10 ml of ethyl alcohol there was added 10 ml of a 13% alcoholic solution of potassium hydroxide, and the mixture was refluxed for 15 minutes. As heating continued, the initial merocyanin gradually dissolved, and a colorless heavy precipitate settled out. The odor of ethylamine was perceptible, and the evolving vapor exhibited an alkaline reaction with litmus. The colorless precipitate was filtered out and washed with 20 ml of absolute alcohol. The resultant product dissolved readily in water, producing a strongly alkaline solution, acidulationof which evolved carbon dioxide. The potassium carbonate weighed 0.42 g (79% of the theoretical), determined by titration with hydrochloric acid in the presence of methylorange. Wash alcohol and 60 ml of water were added to the orange-yellow solution, which grew cloudy when exposed to the air. Air was passed through the solution until no more precipitate was thrown down. The product was filtered out and washed with water until its reaction was neutral. The yield was 0.81 g (66% of the theoretical), m.p. 178-179°. A similar compound was produced by adding hydrogen peroxide to the alkaline solution. The product was purified by crystallizing it from alcohol. Dark-brown prisms with a green tinge. M.p. 179°. Very slightly soluble in water, aqueous alkali, or ether, and rather freely soluble in benzene, alcohol, and chloroform.

Found %: N 9.15, 9.28. $C_{38}H_{36}O_2N_4S_4$. Calculated %: N 9.17.

Acidulating the lemon-yellow mother liquor threw down a light-yellow precipitate (weighing 0.2 g, m.p. 129-134°), which was readily soluble in alcohol and aqueous alkalies.

SUMMARY

1. It has been confirmed that when quaternary salts of dimethinemerocyanins containing a 2-methylmercaptothiazolinone-(4) radical are decomposed in aqueous or alcoholic solution, dyes that are derivatives of thiazolidinedione-(2,4) are formed, the carbonyl-containing ring not being cleaved under these conditions. Thus the reaction involved in the decomposition of these salts, set forth by A. van Dormael, is wrong.

2. It has been shown that when a dimethinemerocyanin containing a thiazolidinedione-(2,4) radical is heated with an alcoholic solution of potassium hydroxide, the carbonyl-containing ring is cleaved, carbon dioxide being split out and an α-mercaptoamide being produced, which is readily oxidized to the respective disulfide.

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* The quaternary salt (I) (V and Y = S; R = C_2H_5) produced by hydrolysis.

** See Consultants Bureau translation, p. 847.

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THE MICROSYNTHESIS OF TAGGED S^{35}-METHIONINE

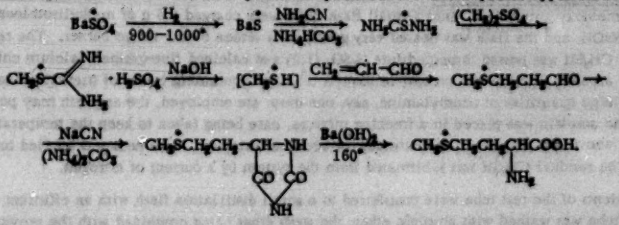
V. I. Malmind, M. N. Shchukina, and T. F. Zhukova

Twenty hears have passed since the initial synthesis of methionine [1], and we now have numerous and varied methods for its synthesis, but only a few of them have been tested for the microsynthesis of S^{35}-methionine.

For example, a check [3] of the Patterson and du Vigneaud method [2] indicated that it was unsatisfactory. The authors subsequently modified their method somewhat [4], raising the methionine yield considerably (38%), based on the barium sulfate, but it still requires special, complicated apparatus, high vacuum (10^{-5}), the use of liquid gases, and the like, and, most important of all, appreciable dilution of the reagents.

Hill and Robson [5] perfected a satisfactory synthesis of methionine, based on elementary sulfur and employing the butyrolactam method. This method involves a large number of stages (up to 19-21), however; moreover, it does not ensure constant high yields of the benzenethiol, which oxidizes readily under the prevailing conditions of the reaction. The best results can be secured, apparently, by starting out with a benzylmagnesium halide and sulfur.

We have worked out a simple method of synthesizing methionine from barium sulfate, making it possible to secure the required quantities of this substance periodically without the use of special apparatus and instruments.



The method is founded upon the addition of methanethiol to acrolein, which is used at present [6] for the synthesis of ordinary methionine. The stage in which thiourea is produced, i.e., the introduction of sulfur into the organic molecule, is of basic importance in this procedure. Though the production of thiourea from hydrogen sulfide or sulfides and cyanamide has been described repeatedly, principally in the patent literature (cf. Kretov's survey [7], for example), these findings cannot be utilized directly, inasmuch as a large excess of hydrogen sulfide is ordinarily used, with the yield calculated in terms of the cyanamide. When stoichiometric proportions of H_2S and cyanamide were employed, the maximum yield did not exceed 60%.

Repeated experiments have shown that when 1.5 moles of cyanamide are used per mole of barium sulfide, the conditions may be so chosen as to ensure complete utilization of the sulfur. The thiourea produced is contaminated by large amounts of dicyandiamide, however, which interfere with the next methylation stage; and purifying the thiourea of the dicyandiamide involves appreciable losses of the former. We found that the thiourea isolated was fully satisfactory for the ensuing reactions when the excess of cyanamide used was no higher than 20%. The thiourea yield then totaled 92% of the theoretical.

In the other stages of the synthesis we found it possible to employ the methods already given in the literature without major finishing processing, as they are applicable without appreciable changes in yields when small quantities are utilized. One exception is the stage in which we produce methylmercaptopropionaldehyde, which does not allow of using quantities below 200 mg without lowering the yield, so that it is advisable to purify it by distillation for use in the subsequent stages. The overall yield of pure methionine averages 26.3% of the theoretical.

We also tried out another method of synthesizing methionine, involving the reaction of methanethiol with β-bromoethylhydantoin [12]. Reacting the resultant (methylmercaptoethyl)-hydantoin with barium hydroxide yields methionine. An advantage of this method is a diminution in the number of stages in which substances containing sulfur are employed. Owing to the instability of the β-bromoethylhydantoin, however, the yields of the (methylmercaptoethyl)-hydantoin fluctuate, rendering the method unreliable.

EXPERIMENTAL

Barium sulfide. The barium sulfate was reduced by the method described in the literature [8]. When the quantity of barium sulfate does not exceed 1.0 g, 75 minutes of heating is all that is necessary. The yield by weight is usually theoretical. Upon titration, the product exhibits a barium sulfite content of 97-99%.

Thiourea. 0.36 gram of pure cyanamide,* 1.2 g of NH_4HCO_3, traces of finely powdered sulfur (less than 0.5 mg), 1.3 g of BaS, and 15 ml of water were placed in a small jar fitted with a well-sealing ground stopper. The mixture was agitated for 2.5 hours at a temperature of 25-30° and then transferred to a long-necked flask and slowly (during the course of an hour) heated to 60°, after which it was brought to a boil, a foam trap connected and a condenser and steam passed through. 25-40 ml of water was driven off until the distillate no longer exhibited an alkaline reaction. The mixture was filtered while still hot, the precipitate being washed with a small quantity of hot water, and the filtrate being evaporated in vacuo to a small volume (2-3 ml). The residue was dried in a vacuum desiccator. The dry substance weighed 0.60 g. M.p. 168-172°. It contained 92% thiourea.

Methylisothiourea sulfate. The method employed was the one described in Syntheses of Organic Preparations [10]. The dimethyl sulfate was first neutralized and distilled. The yield averaged 78%.

Methylmercaptopropionaldehyde. It is convenient to carry this reaction out in a device for the micro determination of methoxy groups [11]. Into a small flask there were charged 0.5 g of methylisothiourea sulfate and 0.72 ml of 5N NaOH, and the flask was heated very gently on a screen over a micro burner. The resultant steady, weak current of CH_3SH was passed through dilute H_2SO_4 (1:2) and calcined fine-grained calcium chloride and then absorbed by the acrolein (1.5-2.0 ml) present in the test tube and containing traces of triethylamine (in a platinum wire loop). (If large quantities of triethylamine, say, one drop, are employed, the acrolein may polymerize.) The test tube with the acrolein was placed in a freezing mixture, care being taken to keep the temperature of the acrolein from rising above -2°. The reaction continued for about 40 minutes. More heat was applied toward the end of the reaction. The residual CH_3SH was sublimated from the system by a current of nitrogen.

The contents of the test tube were transferred to a small distillation flask with an efficient condenser sealed to it. The test tube was washed with absolute ether, the wash ether being combined with the previous mixture. The excess acrolein and ether were driven off at a low vacuum, and the residue distilled. The yield was 0.26 g (70%). B.p. 80° at 30 mm and 66° at 17 mm.

5-(Methylmercaptoethyl)-hydantoin was synthesized by a published method [6]. When small quantities were used, the yield did not exceed 65-70%. M.p. 103-104°.

Methionine [12]. 1.3 grams of finely powdered $Ba(OH)_2 \cdot 8H_2O$ and 0.42 g of (methylmercaptoethyl)-hydantoin, dissolved in 7.7 ml of hot water, were placed in a tube. The tube was sealed and heated in an oscillating bath at 155-165°. The mass solidified within 30 minutes, and heating was discontinued. After the barium carbonate had been suction-filtered out, the filtrate was processed with 0.22 g of ammonium carbonate. The solution was refiltered and then evaporated to dryness in vacuo at 60°. The dry residue was mixed with 2-3 ml of absolute alcohol and suction-filtered. The yield was 0.28 g (93% of the theoretical). Recrystallization from aqueous alcohol yielded 0.22-0.24 g of pure methionine.

SUMMARY

1. A simple method has been developed for synthesizing S^{35}-methionine, starting out with $BaSO_4$, making it possible to work with small quantities of the initial substance.

2. Thiourea, methylisothiourea, methanethiol, and 5-(S-methylmercaptoethyl)-hydantoin containing S^{35} have been synthesized for the first time.

* If the calcium cyanamide is low-grade (35%), we first precipitate calcium cyanamide carbonate, which then gives off CO_2. The solution is carefully evaporated in vacuo, the pure cyanamide being recovered in the usual manner [9].

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DERIVATIVES OF ACETYLENE. 143. HETEROCYCLIC COMPOUNDS

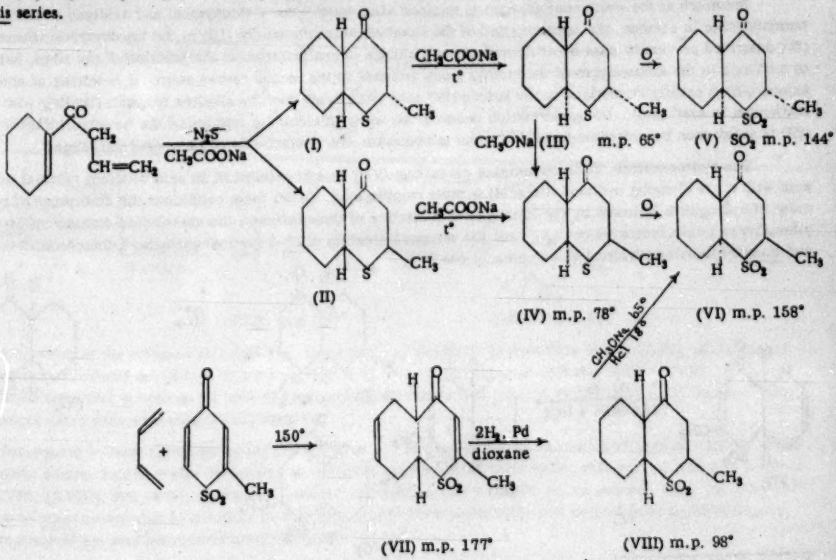
XIX. STERIC ISOMERISM IN THE HYDROGENATED THIOCHROMANONES

I. N. Nazarov, I. A. Gurvich, and A. I. Kuznetsova

As we know, the stereochemistry of bicyclic ketones has been studied in detail, the decalones [1] and the diketodecalins [2] being used as examples. But prior to our researches no research has been done, however, on the stereochemistry of the sulfur analogs of the decalones – the hexahydrothiochromanones and their derivatives – since fully hydrogenated thiochromanones were unknown. The paper by McGinnis and Robinson [3], who isolated two isomers in synthesizing a thiopyranophenanthrene and considered them to be steric isomers, but cited no proof thereof, bears some relationship to the problem in question.

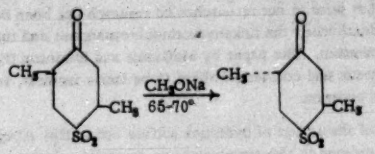
In one of our previous investigations of the action of hydrogen sulfide upon allyl Δ'-cyclohexenyl ketone, we secured 2-methylhexahydro-1-thiochroman-4-one in two stereoisomeric crystalline forms, which yielded the respective stereoisomeric sulfones upon oxidation [4]. We recently undertook the building up of such sulfones by means of a diene condensation of the dioxides of 2-methyl-4-thiopyrones with butadiene [5].

A detailed investigation of the structure of the resultant products indicated that the action of hydrogen sulfide upon allyl Δ'-cyclohexenyl ketone in the presence of sodium acetate results in the formation of trans-2-methylhexahydro-1-thiochroman-4-ones (III) and (IV), yielding upon oxidation the respective trans-sulfones (V) and (VI), differing only in the position of the methyl group attached to the second carbon atom, whereas the bicyclic sulfones (VII), (XV), (XVI), and (XVII), produced by the diene condensation of thiopyrone dioxides with butadiene, belong to the cis series.



It is quite possible that the initial products of the action of hydrogen sulfide upon allyl Δ³-cyclohexenyl ketone are also the cis compounds (I) and (II)*, which are isomerized to the respective trans ketones (III) and (IV) under the conditions governing their formation (heating with sodium acetate).

When the product of diene condensation, (VII), is exhaustively hydrogenated with a Pd catalyst in a dioxane solution, two molecules of hydrogen are absorbed, and the dioxide of cis-2-methylhexahydro-1-thiochroman-4-one (VIII) is produced. When the sulfone (VIII) is boiled in a dilute solution of sodium methoxide or its alcoholic solution is acidulated at room temperature with drops of strong hydrochloric acid, it is irreversibly isomerized to the trans sulfone (VI), which we had previously produced by oxidizing trans-2-methylhexahydro-1-thiochroman-4-one (IV) [4]. That the sulfones (V) and (VI) belong to the trans series is proved by the fact that neither sodium methiodide nor hydrochloric acid is able to isomerize them. Under these conditions cis compounds are completely isomerized to the more stable trans isomers, as has been shown in the monocyclic ketosulfone (IX) [4] as well as in the bicyclic ketosulfone (VIII).



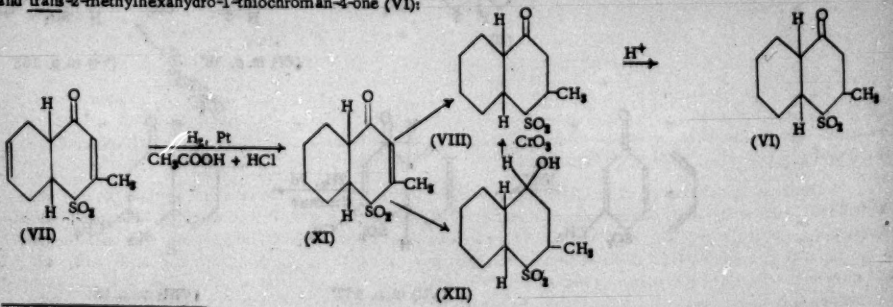
(IX) (X)

It is worthy of note that the unsaturated cis sulfone (VII) cannot be similarly isomerized to the trans compound; it is recovered unchanged after boiling with sodium methoxide or reaction with hydrochloric acid.

As we know, the product of the diene condensation of quinone with one molecule of divinyl is likewise not isomerized even after the conjugated double bond has been reduced, while the product of complete hydrogenation — 1,4-diketodecalin — is readily isomerized to the trans form by enolizing agents [20].

Inasmuch as the steric configuration is retained when tetrahydro-γ-thiopyrones are oxidized to sulfones by permanganate in acetone, the isomerization of the hexahydrothiochromanone (III) to the hexehydrothiochromanone (IV) described previously must be attributed not to a change in configuration at the junction of the rings, but solely to a change in the arrangement of the methyl group attached to the second carbon atom. It is worthy of note that the ketone (III) is readily isomerized to the ketone (IV) only when acted upon by alkaline reagents (boiling with sodium methoxide in methanol). No isomerization occurs at all when an alcoholic solution of the hexahydrothiochromanone (III) is acted upon by hydrochloric acid at room temperature, the substance being recovered unchanged.

The hydrogenation of the unsaturated cis sulfone (VII) by a Pt catalyst in an acid medium (glacial acetic acid with drops of strong hydrochloric acid) is more complicated. Under these conditions the absorption of two molecules of hydrogen is followed by the formation of a mixture of three sulfones: the unsaturated dioxide of cis-2-methylhexahydro-1-thiochromen-4-one (XI), and the saturated dioxides of cis-2-methylhexahydro-1-thiochroman-4-one (XII) and trans-2-methylhexahydro-1-thiochroman-4-one (VI):



(VII) (XI) (VIII) (XII) (VI)

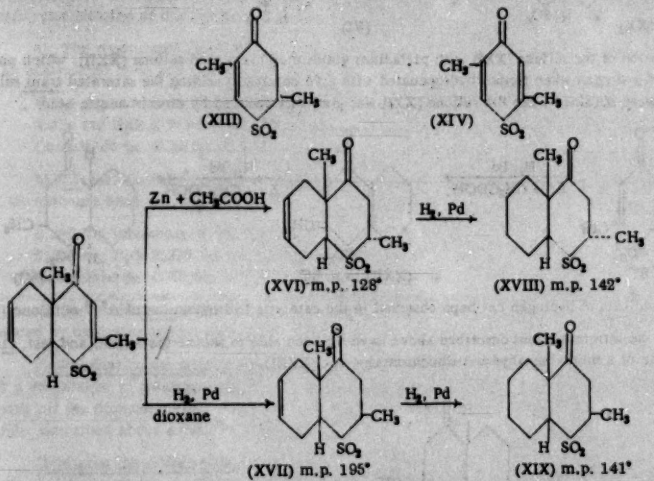
* The position of the methyl groups in the diagram is tentative, since the absolute configuration at C_2 has not been established.

Hydrogenating the sulfone (XI) with a Pd catalyst in dioxane yields the saturated cis sulfone (VIII) described above, which is also produced by the oxidation of the alcohol (XII) with chromic anhydride.

Thus, the sulfone (XI) produced initially is hydrogenated in an acid medium along two different lines: reduction of the carbonyl group (via an unsaturated alcohol) results in the formation of a saturated alcohol (XII), while hydrogenation of the double bond yields the cis sulfone (VIII), which is isomerized by hydrochloric acid at the instant it is formed to the trans ketone (VI). Similar instances of the catalytic hydrogenation of unsaturated ketones have been described in the literature [7]. Our example offers striking proof, however, that a cis ketone (VIII) is not an intermediate product in the formation of the alcohol (XII). Nor is the carbonyl group of two other steric isomers (V) and (VI) hydrogenated by platinum in acetic acid under ordinary conditions.

It is worthy of note that we were unable to secure an intermediate product of the addition of one hydrogen molecule during the partial hydrogenation of the sulfone (VII) with a Pd catalyst in dioxane. This product is apparently hydrogenated faster than the original sulfone. No definite conclusion can be inferred, however, because of the small quantitites of the substance available for our research; there is no doubt, however, that the sulfone (XI) is not produced in this case.

As we have shown in our preceding report [5], condensing the unsaturated sulfone (XIII) with divinyl yields a mixture of two bicyclic cis sulfones (XVI) and (XVII), which differ in the position of the methyl group attached to the second carbon atom. The stereoisomeric sulfones (XVI) and (XVII) are also produced by the partial reduction of the unsaturated bicyclic sulfone (XV), which is produced by the condensation of divinyl with the dioxide of 2,5-dimethylthiopyran (XIV):

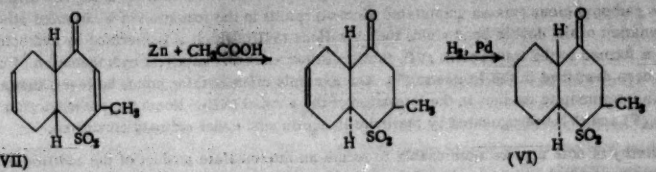


Reduction of the sulfone (XV) with zinc in acetic acid yields the low-melting isomer (XVI), while partial hydrogenation of the sulfone (XV) with a Pd catalyst in dioxane yields the high-melting isomer (XVII). Hence, it is the double bond that is conjugated with the carbonyl group that is first reduced during the partial hydrogenation of the sulfone (XV) with a Pd catalyst in dioxane.

Subsequent hydrogenation of the sulfone (XVI) with a Pd catalyst yields the saturated sulfone (XVIII), while the epimeric sulfone (XVII) yields the respective saturated sulfone (XIX) upon hydrogenation. All the four sulfones (XVI), XVII), (XVIII), and (XIX), produced by diene condensation, are no doubt cis compounds, their inability to isomerize to trans compounds by alkaline or acid catalysts (sodium methoxide and hydrochloric acid) being due to the presence of an angular methyl group alongside the carbonyl.

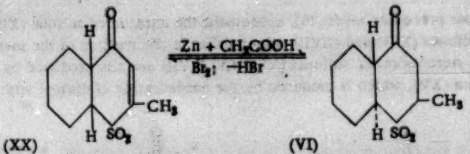
Lastly, we investigated the hydrogenation and reduction of the unsaturated bicyclic sulfones (VII), (XX), and (XXI) described in our preceding report [5], in order to learn the effect of the reaction conditions upon the production of stereoisomers.

Reduction of the cis sulfone (VII), first with zinc in acetic acid and then with hydrogen and a Pd catalyst, yielded the trans sulfone (VI). Inasmuch as hydrogenation with palladium did not change the configuration, the isomerization apparently occurred at the instant the sulfone (VII) was reduced with zinc in acetic acid:



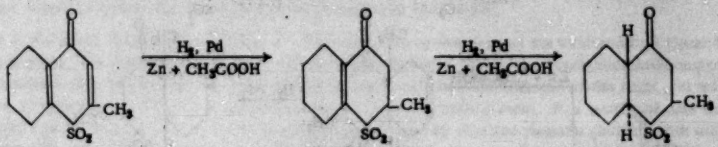
(VII) (VI)

Reduction of the trans sulfone (XX) by zinc in acetic acid or by hydrogen with palladium likewise yielded as the principal product the saturated trans sulfone (VI), from which the unsaturated sulfone (XX) is secured by bromination and splitting off hydrogen bromide:



(XX) (VI)

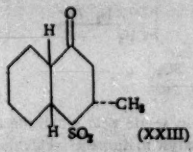
Partial hydrogenation of the sulfone (XXI) with palladium yields the unsaturated sulfone (XXII), which undergoes the trans addition of hydrogen when further hydrogenated with a Pd catalyst, yielding the saturated trans sulfone (VI). The same results were obtained when the sulfone (XXI) was gradually reduced by zinc in acetic acid:



(XXI) m.p. 87° (XXII) m.p. 85° (VI)

A similar trans addition of hydrogen has been observed in the catalytic hydrogenation of $\Delta^{9,10}$-octalone [8].

Thus, in none of the transformations described above have we been able to secure the fourth, and last, cis steroisomer of the dioxide of 2-methylhexahydro-1-thiochroman-4-one (XXIII).



(XXIII)

When we hydrogenated the diene condensation product (VII) and the sulfones (XX) and (XXI) under various conditions, not only did we fail to obtain the cis sulfone (XXIII), but we also failed to get its trans form (V). The steric arrangement of the methyl group in the sulfones (VI) and (VII I) is evidently the more stable form.

EXPERIMENTAL

Hydrogenation of the sulfone (VII) in a neutral medium. 0.6 gram of the sulfone (VII) (m.p. 176-177°) [5] was hydrogenated with a Pd catalyst * in a dioxane solution. 63 ml of hydrogen was absorbed in 2 hours, after which the mixture was heated to 50° for 3 hours, another 74 ml of hydrogen being absorbed. Thus, a total of 137 ml of

* Palladium oxide on calcium carbonate was employed in every test.

hydrogen at 18° and 745 mm was absorbed (two molecules). The catalyst was filtered out and the dioxane driven off, the residue crystallizing. Triple recrystallization from a benzene-petroleum ether and then from gasoline yielded colorless needles of the cis sulfone (VIII), readily soluble in alcohol, water, acetone, and benzene, with an m.p. of 98°.

4.412 mg substance: 8.995 mg CO_2; 2.895 mg H_2O; 1.945 mg SO_4. Found %: C 55.64; H 7.34; S 14.71. $C_{10}H_{16}O_3S$. Calculated %: C 55.53; H 7.46; S 14.83.

Isomerization of the cis sulfone (VIII) to the trans sulfone (VI). a) 0.1 gram of the cis sulfone (VIII) (m.p. 98°) was dissolved in 0.5 ml of methanol containing 0.1% sodium and then boiled for two hours. As the solution cooled, crystals settled out; their m.p. was 157.5-158° after a single recrystallization from alcohol, and their mixed melting point with the trans sulfone (VI) produced by oxidizing 2-methylhexahydro-1-thiochroman-4-one (IV) [4] exhibited no depression.

b) 0.1 gram of the cis sulfone (VIII) (m.p. 98°) was dissolved in 3 ml of 96% ethyl alcohol, and two drops of strong hydrochloric acid were added to the solution. Three days later the crystals that had settled out were recrystallized from alcohol; their m.p. was 157-158°, and their mixed melting point with the trans sulfone (VI) was also 157-158°.

Hydrogenation of the sulfone (VII) in an acid medium. 1 gram of the sulfone (VII) was hydrogenated in 20 ml of acetic acid by platinum oxide, with two drops of strong hydrochloric acid added to the solution. During 2 hours 240 ml of hydrogen at 18° and 750 mm (two molecules) were absorbed, after which the rate of hydrogenation dropped sharply. Driving off the solvent in vacuo yielded a mixture of crystals with an m.p. of 110-120°. Fractional crystallization of this mixture from alcohol yielded three substances:

a) The unsaturated cis sulfone (XI) with an m.p. of 130.5° (from alcohol); the substance exhibited a reaction for an unsaturated bond with permanganate.

5.210 mg substance: 10.647 mg CO_2; 3.022 mg H_2O. 2.270 mg SO_4. 4.919 mg substance: 10.052 mg CO_2; 2.820 mg H_2O; 2.180 mg SO_4. Found %: C 55.77, 55.77; H 6.49, 6.41; S 14.55, 14.80. $C_{10}H_{14}O_3S$. Calculated %: C 56.05; H 6.58; S 14.96.

b) Cis sulfone (XII) – lustrous needles, m.p. 140-140.5° (from an acetone-ether mixture); the permanganate test for a double bond was negative.

4.325 mg substance: 8.745 mg CO_2; 3.245 mg H_2O; 1.885 mg SO_4. 5.230 mg substance: 10.570 mg CO_2; 3.965 mg H_2O; 2.325 mg SO_4. Found %: C 55.18, 55.15; H 8.39, 8.48; S 14.55, 14.84. $C_{10}H_{16}O_3S$. Calculated %: C 55.01; H 8.31; S 14.69.

c) Saturated trans sulfone (VI) with an m.p. of 158°, exhibiting no depression when mixed with a sample produced by oxidizing trans-2-methylhexahydro-1-thiochroman-4-one (IV) with permanganate [4].

Hydrogenating the sulfone (XI). 0.15 gram of the sulfone (XI), with an m.p. of 130°, was hydrogenated with a Pd catalyst in a dioxane solution. 17 ml of hydrogen at 20° and 751 mm (one molecule) was absorbed. Driving off the dioxane yielded the cis sulfone (VIII) with an m.p. of 98°, whose mixed melting point with the sample described above exhibited no depression.

Oxidizing the sulfone (XII) with chromic anhydride. A solution of 0.04 g of chromic anhydride in glacial acetic acid was added to a solution of 0.118 g of the sulfone (XII) in 5 ml of glacial acetic acid. Two days later, 5 drops of alcohol was added to reduce the excess chromic anhydride, and the solvent was driven off. Ether and benzene were added, and the mineral precipitate was filtered out of the solution. Fleecy needles (about 100 mg) with an m.p. of 98-98.5° were formed on the walls of the flask when the solvent was evaporated. Their mixed melting point with the sulfone (VIII) exhibited no depression.

Partial hydrogenation of the sulfone (VII) with a Pd catalyst in a neutral medium. 100 mg of the sulfone (VII) (m.p. 177°) was hydrogenated with a Pd catalyst in 6 ml of dioxane. 12.5 ml of hydrogen at 19° and 754 mm (one molecule) being absorbed in 15 minutes. Driving off the solvent yielded about 50 mg of the original sulfone (mixed melting point showed no depression). Then hydrogenation was continued, another 10 ml of hydrogen being absorbed. Driving off the solvent yielded the hydrogenation end product, with an m.p. of 98°, the mixed melting point with the sulfone (VIII) exhibited no depression. Repeating the experiment with the same quantities of the original product yielded the same results.

Reducing the sulfone (VII) with zinc in acetic acid. 1 gram of the sulfone (VII) (m.p. 177°) and 10 ml of glacial acetic acid were boiled for two hours with 1 g of zinc dust. After the mixture had cooled, the zinc was filtered out, and hydrogen sulfide was passed through the solution. The precipitate was filtered out, and the acetic acid driven off in vacuo; this yielded 200 mg of crystals with an m.p. of 173-174°, whose mixed melting point with the original sulfone exhibited no depression. The residue consisted of 0.7 g of an oil, which was thoroughly hydrogenated with a Pd catalyst in dioxane. It absorbed 120 ml of hydrogen at 19° and 752 mm (one and a half molecules). Driving off the dioxane yielded 0.25 g of the trans sulfone (VI) with an m.p. of 156-157° (from alcohol), whose mixed melting point with a known sample [4] exhibited no depression. We were unable to investigate the remaining oil (370 mg).

Hydrogenating the sulfone (XXI). 1.62 grams of the sulfone (XXI) (m.p. 87°) [5] was hydrogenated with a Pd catalyst in an alcohol-acetone mixture. In 5 hours 187.4 ml of hydrogen at 20.5° and 745 mm (one molecule) was absorbed. The solvent was driven off and ether was added, yielding 600 mg of crystals with an m. p. of 80-82°. Triple recrystallization from ether yielded the sulfone (XXII) with an m.p. of 85-85.5°.

4.920 mg substance: 10.090 mg CO_2; 2.875 mg H_2O; 2.160 mg SO_4. Found %: C 55.96; H 6.64; S 14.65. $C_{18}H_{24}O_2S$. Calculated %: C 56.05; H 6.58; S 14.96.

The substance exhibited a double-bond reaction with permanganate. Its mixed melting point with the original sulfone (XXI) was 71-78°. The residual oil yielded individual crystals of a higher-melting unsaturated substance.

Reducing the sulfone (XXI) with zinc dust. a) 0.5 gram of the sulfone (XXI) (m.p. 87°), 6 ml of glacial acetic acid, and 0.7 g of zinc dust were refluxed for three hours. The precipitate was filtered out and the solvent driven off, yielding crystals with an m.p. of 84-85° (from ether), whose mixed melting point with the sulfone (XXII) described above exhibited no depression.

b) 0.4 gram of the sulfone (XXI) (m.p. 87°) was refluxed for 1.5 hours with 1.2 g of zinc dust, activated by hot dilute hydrochloric acid, and 5 ml of acetic acid. Driving off the solvent yielded crystals of the trans sulfone (VI) with an m.p. of 156-157° (from alcohol). Their mixed melting point with a known sample exhibited no depression.

Hydrogenating the sulfone (XXII). 0.3 gram of the sulfone (XXII) (m.p. 85°) was hydrogenated with a Pd catalyst in 6 ml of an alcohol-ether mixture; 48 ml of hydrogen at 19° and 752 mm (one molecule) was absorbed. The resultant crystals had an m.p. of 156-157° after double recrystallization from alcohol. Their mixed melting point with the trans sulfone (VI) described above was 157-158°.

Reducing the sulfone (XX). a) 0.2 g of the sulfone (XX) (m.p. 118°) [5] was hydrogenated with a Pd catalyst in a dioxane solution, 24.8 ml of hydrogen at 23° and 747 mm (one molecule) being absorbed within 1 hour. Driving off the dioxane yielded crystals with an m.p. of 153-154°. Recrystallization from alcohol yielded the trans sulfone (VI), with an m.p. of 157°. Its mixed melting point with a known sample was 156-157°.

b) 0.6 gram of the sulfone (XX) (m.p. 118°), 5 ml of acetic acid, and 0.6 g of zinc dust were refluxed for 2 hours. The solvent was driven off, yielding 0.2 g of crystals of the trans sulfone (VI) with an m.p. of 157-158° (from alcohol), whose mixed melting point with a known sample exhibited no depression. The residue, a gradually crystallizing oil, was not investigated.

Reducing the sulfone (XV) with zinc dust. 0.22 gram of the sulfone (XV) (m.p. 100-102°) [5], 0.29 g of zinc dust, and 2.2 ml of acetic acid were refluxed for 1 hour. After the mixture had cooled, the zinc was filtered out, and the acetic acid driven off in vacuo, the residue being recrystallized from alcohol. This yielded 0.05 g of crystals of the sulfone (XVI) with an m.p. of 127-128°, whose mixed melting point with a known sample, produced by diene synthesis [5], exhibited no depression.

Hydrogenating the sulfone (XV). a) 0.15 gram of the sulfone (XV) (m.p. 101-102°) [5] was dissolved in 6 ml of dioxane and hydrogenated with a Pd catalyst, 16.7 ml of hydrogen at 20° and 742 mm (one molecule) being absorbed within half an hour. The catalyst was filtered out and the dioxane driven off, whereupon the residue crystallized. Recrystallization from alcohol yielded the sulfone (XVII) with an m.p. of 194°. Its mixed melting point with a known sample, produced by diene synthesis [5], was 194-195°.

b) 0.68 g of the sulfone (XV) (m.p. 101-102°) was dissolved in 10 ml of dioxane and hydrogenated with a Pd catalyst at 80°, 145.8 ml of hydrogen at 20° and 753 mm (two molecules) being absorbed. The dioxane was driven off and the residue recrystallized three times from an alcohol-ether mixture. This yielded the saturated sulfone (XIX) as needles with an m.p. of 140.5-141.5°

5.830 mg subs.: 12.254 mg CO_2, 4.020 mg H_2O; 2.405 mg SO_2. Found %: C 57.36; H 7.71; S 13.77. $C_{11}H_{16}O_3S$. Calculated %: C 57.37; H 7.88; S 13.92.

Hydrogenating the sulfone (XVI). 0.45 g of the sulfone (XVI) (m.p. 126-127°) was hydrogenated with a Pd catalyst in 10 ml of alcohol, 50 ml of hydrogen at 22° and 749 mm (one molecule) being absorbed within 1 hour. Driving off the solvent, followed by double recrystallization from alcohol, yielded the sulfone (XVIII), with a m.p. of 142-142.5°.

3.770 mg subs.: 7.742 mg CO_2; 2.615 mg H_2O; 1.560 mg SO_2. Found %: C 57.35 H 7.94; S 13.91. $C_{11}H_{16}O_3S$. Calculated %: C 57.37; H 7.88; S 13.92.

The mixed melting point of the sulfone (XVIII) and its isomeric sulfone (XIX) was 107-118°.

The epimeric cis sulfones (XVIII) and (XIX) are not isomerized to the respective trans sulfones at all, whether by boiling with sodium methoxide in methanol or by the action of strong hydrochloric acid on their alcoholic solutions at room temperature. Both of these sulfones were recovered completely unchanged.

SUMMARY

1. Stereoisomerism in several hydrogenated thiochromanone derivatives and the respective sulfones has been investigated for the first time.

2. The previously synthesized trans sulfones (V) and (VI) have been supplemented by the cis sulfone (VIII), synthesized by a diene condensation, which is readily isomerized to the trans isomer (VI) by sodium methoxide or hydrochloric acid.

3. The epimeric cis sulfones (XVI) and (XVII) have been synthesized by the partial hydrogenation of the sulfone (XV) under different conditions; further hydrogenation of these sulfones yielding the respective saturated cis sulfones (XVIII) and (XIX). The latter cannot be isomerized to trans compounds because of the presence of an angular methyl group alongside the carbonyl.

4. The hydrogenation of the unsaturated sulfones (VII), (XX), (XXI), and (XXII), has been investigated under various conditions.

5. It has been shown that the sulfone (VII) is hydrogenated in an acid medium along two independent lines, yielding a mixture of the sulfones (VI), (XI), and (XII).

6. When the sulfones (XV) are partially hydrogenated with a Pd catalyst in dioxane, the double bond conjugated with the carbonyl group is the first to be reduced.

7. When the double bond between the rings is reduced in the sulfone (XXII), trans addition of hydrogen takes place.

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THE CHEMISTRY OF THE OILS OF FRESH-WATER FISH

III. THE COMPOSITION OF THE OIL IN THE TISSUES OF PERCA SHRENKI KESSL.

M. N. Chechenkin

Climate, the living conditions of organisms, the nature of their food, and other factors affect the chemical composition of animal and vegetable fats. Pigulevsky [1], and after him Ivanov [2], long ago established the relationship between climate and the unsaturation of linseed oil. The more severe the climatic conditions in which the plant grew, the higher the unsaturation of the oil. Terroine [3] extended these conclusions to animal fats. The influence of different living conditions of organisms upon the chemical composition of their fats has been noted by Jolson [4], Ellis [5], Brown [6], Kizeveiter [7], Goldovsky [8], and Hilditch [9].

At the same time, however, it is known that the chemical composition of the fats is more or less constant for related groups of plant and animal organisms.

The present research was carried out to ascertain the effect of external conditions upon a change in the chemical composition of the oils of fresh-water fish, with special emphasis upon changes in their acid composition.

There is only one other species of the perch family native to the USSR, the Lake Balkash perch Perca schrenki Kessl, besides the river perch, Perca fluviatilis L. [10], samples of which were taken from the Pskov-Chuda reservoir. The range of temperatures prevailing at the Pskov-Chuda fresh-water reservoir is extremely wide. Lake Balkhash, a partially salt lake, the mean temperature of whose water in July is +24.0°, its maximum temperature being +27.7°, with the temperature difference between the bottom and surface water never exceeding 3.5°, is not completely frozen over every winter [11]. It is obvious that the geographical, physicochemical, and other conditions of life are thus quite different for these two species of fish, which are very closely related genetically.

The results of our comparative investigations of the oils in the tissues of Perca schrenki and Perca fluviatilis proved to be highly interesting. To begin with, the composition of the tissue fats of the Balkhash perch exhibits a lesser degree of unsaturation of the highly unsaturated acids. A very typical feature of the tissue oils of the perch, as of all fish in general – the presence of highly unsaturated (clupanodonic) acids, with four and five double bonds – also holds true for the tissues of the Balkhash perch. But in contrast to the oil of Perca fluviatilis, in which the most characteristic acid is clupanodonic acid, $C_{22}H_{34}O_2$, with five double bonds, the typical acid in the tissue oils of Perca schrenki is terapinic acid (formerly called clupanodonic acid) $C_{18}H_{28}O_2$, with four double bonds. The highest content of terapinic acid is found in the roe (up to 15%), with the lowest figure found in the oil of the viscera (up to 9%). Clupanodonic acid is found only in the oil of the liver of Perca schrenki. Clupanodonic acid is not typical of the oils in all the other tissues of Perca schrenki, its place being taken by a less highly unsaturated acid: terapinic acid.

Of the other highly unsaturated acids, arachidonic acid, $C_{20}OH_{32}O_2$, with four double bonds, has been found in the oils of Perca schrenki tissues (no less than 5%).

The bulk of the oils in all the tissues of Perca schrenki consists of oleic acid, constituting as much as 50% of the total acid mixture – thus resembling the acid structure of Perca fluviatilis. In their percentages of saturated acids and unsaponifiable fats, the tissues of Perca schrenki resemble the oils of the corresponding tissues of Perca fluviatilis.

Analysis of the oils in the Balkhash perch indicates that the highly unsaturated acids are the most highly mobile material in the oils of fresh-water fish. The external factors operate chiefly to alter the degree of unsaturation of these acids. The diminution of the unsaturation of the highly unsaturated acids in the oils of Perca schrenki must be attributed principally to the higher prevailing temperature in Lake Balkhash. The Michurin doctrine of the influence of the medium upon the various structural features of the living organism also applies to the chemical composition of the oils in the different tissues of fresh-water fish.

Contrary to the findings of O.B.Maximov [12], no liquid bromides are produced by the repeated bromination and debromination of the bromides in Fraction I, which are derivatives of highly unsaturated acids. Repeated bromination and debromination always yields approximately equal quantities of two types of bromides: 1) bromides that are insoluble in diethyl ether, and 2) bromides that are soluble in diethyl ether under the prevailing bromination conditions (mother-liquor bromides). The latter, which are pasty at first, turn out to be solids – derivatives of highly unsaturated acids – after extraction from the solution and drying in vacuo, though their bromine content is diminished, to be sure.

The separation of the ether-insoluble bromides of Fraction I into insoluble and soluble bromides by means of repeated bromination and debromination must be attributed to the fact that repeated alternating bromination and debromination results in the formation of soluble bromides with a lower percentage of bromine. O.B.Maximov gives a survey of numerous conflicting findings on the nature of the mother-liquor bromides secured by the repeated bromination and debromination of the bromides of highly unsaturated acids, together with varying interpretations of this phenomena [12].

Research on the bromides in various fractions and on the products of their debromination give no indication that the ordinary unsaturated acids, linoleic and linolenic acids, are present in the tissues of either Perca schrenki or Perca fluviatilis [10].

EXPERIMENTAL

The oils were extracted from the fish tissues, their constants were determined, the oils were saponified, the free acids were isolated, the acid mixtures were brominated, and the bromides were separated into a total of eight fractions for all the tissues of Perca schrenki exactly as described in our previous report [10]. The important Fraction VI of (liquid) bromides was secured from a separate batch of oil by first separating out the unsaponifiable solid acids, hydroxy acids, and the like, as described in [10]. The constants of the oils of the carcass, the head, the viscera, the roe, and the liver (in January) are given in Table 1.

TABLE 1

Constants of the Oils in the Tissues of Perca schrenki

Tissue	% Oil	Acid No.	Saponification No.	Iodine No.	Percentages					d_4^{15}
					Solid acids (Twitchell method)		Polybromides, %	Unsaponifiables, %	Ash, %	
					%	Iodine No.				
Carcass	8.02	13.29	185.90	131.0	16.62	5.50	21.66	3.45	–	0.9332
Head	18.15	13.81	184.69	127.18	15.16	5.11	17.93	4.67	0.11	0.9306
Viscera	46.0	18.1	192.08	120.50	17.43	8.05	16.80	1.44	0.05	0.9350
Liver	12.8	–	–	136.67	19.2	–	21.0	5.20	–	–
Roe	23.02	14.29	120.27	138.64	10.60	37.30	17.06	29.49	0.40	0.9032

Composition of the Oil in the Carcass of Perca schrenki

When the bromides of Fractions I, II, III, and V were heated, the color gradually changed to a pure black, but without any sign of melting. The bromides turned completely black at 200°, remaining unchanged when heated to 240° and above. The bromides of Fractions I and II darkened evenly, the darkening of the bromides in Fraction III being uneven. This was evidence that the bromides in Fractions I and II were homogeneous, while those in Fraction III were nonhomogeneous. All the fractions of solid bromides, including those soluble in diethyl ether under the conditions of bromination (Fraction V), were derivatives of highly unsaturated acids. It should be noted that everything that is said about the melting points of the solid bromides derived from the acids in the carcass oil applies to the melting of the respective bromides from the acids in the oils of all the other tissues.

The presence of bromine was always determined by the Carius method; the analysis results are given in Table 2. The per cent yield of the bromides was based on the acid mixture used for bromination.

Fraction IV of the bromides was not collected because of the negligible quantity yielded by this tissue as well as by all the other tissues.

TABLE 2

Per Cent Bromine in Bromides Obtained from the Acids in the Oil of the Carcass of Perca schrenki

Bromide fraction	% Yield of bromides	% Bromine
I	21.66	69.48, 69.73
II	2.10	68.72, 68.43
III	8.80	67.56, 67.51
V	2.63	67.60, 67.73
VI	98.92	50.11, 50.11
VII	7.84	36.68, 36.41
VIII	4.39	42.22, 42.00

We see in Table 2 that: 1) the percentage of bromine in Fraction I of the bromides does not correspond to the decabromide of clupanodonic acid; 2) the bromides of all the benzene fractions, I, II, and III, as well as the bromides of Fraction V, soluble in diethyl ether under the bromination conditions, are derivatives of highly unsaturated acids that are characteristic of the oils in all the tissues of Perca schrenki, as in all fish oils; 3) the liquid bromides of Fraction VI dissolve an especially large quantity of solid bromides, which explains the higher percentage of bromine; 4) the bromides of Fraction VII are derivatives of oleic acid; Fraction VII is the same as Fraction VI, but more highly refined.

Debromination of Fraction I bromides. 7.73 g of the bromides, 6 g of zinc dust, and 25 ml of anhydrous pyridine were refluxed in a current of CO_2 on a 65-70° water bath for 6 hours, using a stirrer. The acid was extracted with ether, the ether extract being treated with 10% HCl to remove the pyridine, washed with water until the reaction for the Cl ion was negative, and dried with anhydrous Na_2SO_4. The ether was driven off and the acid dried in a 10-15 mm vacuum on a water bath at 50-55°. The acid yield was 2.07 g (88.8% of the theoretical, based on terapinic acid, $C_{18}H_{28}O_2$).

The iodine number of the acid was determined by the Hübl method, as was our practice throughout, the iodine number being found to be 357.40, 357.80. This iodine number could be taken as that of clupanodonic acid, $C_{22}H_{34}O_2$, if not for the lowered percentage of bromine in the prospective bromides; in debrominating the Fraction I bromides in various tissues of Perca fluviatilis [10] with a bromine content of 70.21-70.33%, we obtained an acid that we took to be clupanodonic acid, which had approximately the same iodine number.

The molecular weight of the acids was always determined by titrating a weighed sample of the acid dissolved in 50 ml of a neutralized 1:1 mixture of absolute ether and benzaldehyde alcohol with a 0.1 N alcoholic solution of KOH and 0.5 ml of a 1% solution of thymolphthalein.

Found: M 347.58, 346.91.

The experimental molecular weight is higher than the value calculated theoretically for terapinic acid (276.22) or for clupanodonic acid (330.27). The carboxyl group is apparently somewhat esterified.

Bromination of the debromination product. 0.88 g of the acid was brominated in 70 ml of anhydrous ether under the usual conditions. The precipitate was suction-filtered, washed with ether until all the excess bromine had been removed, and dried in a vacuum desiccator over Na_2SO_4. This constituted the insoluble (solid) bromides (120% yield). The ether filtrate was processed with a solution of $Na_2S_2O_3$, washed with water, and dried with anhydrous Na_2SO_4; driving off the solvent yielded the mother-liquor bromides as a pasty mass, which was dried in a vacuum desiccator over anhydrous Na_2SO_4. The mother-liquor bromides foamed as the air was drawn out, the foam rapidly solidifying, solid white bromides being produced. These constituted the soluble (mother-liquor) bromides (124% yield). The soluble (mother-liquor) bromides were recovered from all the solid bromide fractions and from all the tissues by this procedure. Henceforth, these bromides will be called soluble instead of "liquid" throughout, the first group of bromides being called insoluble instead of "solid". About the same quantity was obtained from all the tissues. Eibner's assertion [13] that the debromination product of the Fraction I bromides are quantitatively converted into the decabromide by bromination is not borne out by our findings; the original product constitutes only 50%, the other 50% consisting of bromides with a lower percentage of bromine.

The insoluble bromides do not melt when heated, but they do turn black. The soluble (mother-liquor) bromides have sharp melting points, though it is extremely difficult to detect the onset of fusion. In all cases, the melting point has been taken as the appearance of minute droplets with silvery reflections, barely perceptible with a magnifying glass. In the present instance the m.p. of the bromides was 60-61°.

Per cent bromine in the insoluble bromides. Found: 69.11, 69.51. $C_{18}H_{28}O_2Br_8$. Calculated %: Br 69.83.

Per cent bromine in the soluble bromides: 66.10, 65.96.

Debromination of the Fraction III bromides. We took 2.62 g of the bromides, 5 g of zinc dust, and 9 ml of pyridine. The acid yield was 0.78 g (92.85% of the theoretical, based on arachidonic acid, $C_{20}H_{32}O_2$). All of this acid was brominated, yielding: 1) 0.85 g (109.0%) of insoluble (solid) bromides; and 2) 0.92 g (118.0%) of soluble (mother-liquor) bromides.

The insoluble bromides did not melt; the soluble bromides melted at 50°.

Per cent bromine in the insoluble bromides: Found 68.44, 69.21. The per cent bromine is higher than that in the original Fraction III bromides.

Per cent bromine in the soluble bromides: Found 65.32, 65.53.

Debromination of Fraction VI. We took 9 g of the bromides, 6 g of zinc dust, and 27 ml of pyridine. The yield was 3.65 g of acid, which was saponified with 20 ml of 0.5 N alcoholic KOH, the potassium salts being treated with 15 ml of petroleum ether and then decomposed with 7 ml of 5 N H_2SO_4. This yielded 3.19 g of acid.

Found: iodine number 128.00, 128.56; M 301.89, 300.40.

Bromination of the product of debrominating Fraction VI. 1.82 g of the acid was dissolved in 30 ml of petroleum ether, the turbidity was filtered out, and the filtrate was brominated in the usual manner. The bromide precipitate was suction-filtered, washed with petroleum ether, and dried in a vacuum desiccator over anhydrous Na_2SO_4. The yield of insoluble solid bromides totaled 0.65 g (35.72%, based on the acid). The filtrate was treated with a $Na_2S_2O_3$ solution, washed with water, and dried over anhydrous Na_2SO_4, the petroleum ether being driven off on a water bath; the remaining liquid bromides were dried in vacuo at 10-15 mm and 50-55°. The liquid bromides were a beautiful light-brown; the yield was 2.50 g (137.3%, based on the acid).

Per cent bromine in the solid bromides: Found 56.86, 56.64.

Per cent bromine in the liquid bromides: Found 45.10, 45.39.

Oleic acid from the Fraction VII bromides. The per cent bromine in the Fraction VII bromides (36.55%) is very close to the per cent bromine in the dibromide of oleic acid (36.18%). We took 2.1 g of the bromides, 3.5 g of zinc dust, and 8 ml of pyridine. We obtained 0.48 g of acid (35.82%, based on oleic acid). The acid was not saponified, but was brominated in 15 ml of petroleum ether. The bromine yield was as follows: 1) solid 0.05 g (20.4%); 2) liquid 0.75 g (156.2%).

Per cent bromine in the liquid bromides: Found 36.20, 36.25. $C_{18}H_{34}O_2Br_2$. Calculated %: Br 36.18.

It is obvious that the Fraction VII bromides were derivatives of oleic acid. The Fraction VI bromides were likewise derivatives of oleic acid, for Fraction VII was the same as Fraction VI, merely better refined.

Composition of the Head Oil of Perca schrenki

The physicochemical constants of the head oil are given in Table 1; the per cent bromine in the bromides of the oil acids is given in Table 3.

TABLE 3

Per Cent Bromine in Bromides Obtained from the Acids in the Head Oil of Perca Schrenki

Bromide fraction	% Yield of bromides	% Bromine
I	17.93	69.28, 69.39
II	2.23	68.00, 68.29
III	13.28	67.03, 67.47
V	1.80	66.01, 66.49
VI	132.0	52.21, 51.96
VII	9.34	45.09, 45.35

As we see in Table 3, the Fraction VI and VII bromides contain an unusually high proportion of bromides of the benzene fractions.

Terapinic acid from the Fraction I bromides. 6.82 g of bromides, 5 g of zinc dust, and 25 ml of pyridine. The acid yield was 1.90 g (92.70%, based on terapinic acid, $C_{18}H_{28}O_2$). Determination of the molecular weight yielded values that were too high: 280.90; 381.60.

Found iodine number: 321.62, 321.09.

Bromination of terapinic acid obtained from Fraction I. 0.9 g of the acid was dissolved in 30 ml of ether and then brominated. The bromide yield was as follows: 1) insoluble 1.0 g (111.1%); 2) soluble 1.2 g (133.3%).

Per cent of bromine in the insoluble bromides: Found 69.55, 69.37. $C_{18}H_{28}O_2Br_8$. Calculated %: Br 69.83.

Per cent bromine in the soluble bromides: Found 68.28, 68.00.

Oleic acid from the Fraction VI bromides. We took 12 g of the bromides, 8 g of zinc dust, and 36 ml of pyridine. The acid yield was 4.2 g (54.90%, based on oleic acid). The debromination product was saponified before analysis as described above; the yield was 3.6 g (47.0%).

Found: iodine number 116.10, 116.42, M 308.60, 307.70.

Bromination of the oleic acid secured from Fraction VI. 0.91 g of the acid was dissolved in 20 ml of petroleum ether; the bromination, isolation of the bromides, and their preparation for analysis were all as described above. The bromide yield was as follows: 1) solid 0.12 g (13.18%); 2) liquid 1.13 g (124.2%, based on the acid).

TABLE 4

Per Cent Bromine in Bromides Obtained from the Acids in the Oil of the Viscera of Perca schrenki

Bromide fraction	% Yield of bromides	% Bromine
I	16.80	69.43, 69.22
II	4.34	67.76, 67.85
III	7.07	67.50, 67.67
V	2.18	68.78, 68.60
VI	97.2	43.79, 43.32
VII	3.40	40.80, 40.90
VIII	1.6	48.09, 48.09

TABLE 5

Per Cent Bromine in Bromides Obtained from the Acids in the Oil of the Viscera of Perca fluviatilis

Bromide fraction	% Bromine
I	70.46, 70.47
II	68.09, 68.37
III	66.08, 65.70
V	67.88, 67.93
VI	41.75, 41.66
VII	43.70, 44.11
VIII	57.31, 57.54

Per cent bromine in the solid bromides: Found 53.25.

Per cent bromine in the liquid bromides: Found 46.00, 46.15.

Composition of the Oil in the Viscera of Perca schrenki

The constants of the viscera oil are given in Table 1; the per cent bromine in the bromides of all the fractions of the oil acids is given in Table 4.

In Table 5 we cite for the sake of comparison the per cent bromine in the bromides obtained from the acids in the fat of the viscera of Perca fluviatilis.

Terapinic acid from the Fraction I bromides. We took 6.20 g of the bromides, 5 g of zinc dust, and 20 ml of pyridine. The reaction lasted 6 hours, the acid yield totaling 1.59 g (85.03% of the theoretical, based on terapinic acid, $C_{18}H_{32}O_2$).

Found: iodine number 352.4, 352.6.

Bromination of the terapinic acid obtained from Fraction I. We took 1.16 g of the acid in 50 ml of diethyl ether. The bromide yield was as follows: 1) insoluble 1.81 g (156.0%); 2) soluble 1.80 g (155.2%). The soluble bromides had a m.p. of 59-60°.

Per cent of bromine in the insoluble bromides: Found 69.36, 69.43. $C_{18}H_{32}O_2Br_8$. Calculated %: Br 69.83.

Per cent bromine in the soluble bromides: Found 67.53, 67.20.

Redebromination of the insoluble bromides. We took 1.50 g of the bromides, 3 g of zinc dust and 9 ml of pyridine. The acid yield was 0.40 g (88.8%, based on terapinic acid). 0.33 g of this acid was brominated in 15 ml of diethyl ether. The bromide yield was as follows: 1) insoluble 0.45 g (136.37%); 2) soluble 0.47 g (142.42%).

Per cent bromine in the insoluble bromides: Found 69.30, 69.19. $C_{18}H_{32}O_2Br_8$. Calculated %: Br 69.83.

Per cent bromine in the soluble bromides: Found 66.66, 66.90.

Arachidonic acid from the Fraction II bromides. 1.50 g of the bromides, 3 g of zinc dust, and 9 ml of pyridine. The acid yield was 0.36 g (75.0%, based on arachidonic acid, $C_{20}H_{32}O_2$, the octabromide of which contains 67.75% bromine). The acid was brominated in 25 ml of diethyl ether. The bromine yield was as follows: 1) insoluble 0.37 g (102.8%); 2) soluble 0.40 g (111.1%). The m.p. of the soluble bromides was 56-57°.

Per cent bromine in the insoluble bromides: Found 68.00, 67.52.

Per cent bromine in the soluble bromides: 63.87, 63.70.

Arachidonic acid from the Fraction III bromides. We took 2.90 g of the bromides, 5 g of zinc dust, and 12 ml of pyridine. The acid yield was 0.88 g (93.62% of the theoretical, based on arachidonic acid, $C_{20}H_{32}O_2$.)

The acid was brominated in 40 ml of diethyl ether. The bromide yield was as follows: 1) insoluble 1.03 g (113.04%); 2) soluble 1.40 g (159.1%).

The m.p. of the soluble bromides was 49-50°.

Per cent bromine in the insoluble bromides: Found 69.14, 69.30. The high bromine percentage cannot be reconciled with the other findings, though an experimental error is out of the question, since two more analyses yielded the same results.

Per cent bromine in the soluble bromides: Found 65.21, 65.02.

Oleic acid from the Fraction VI liquid bromides. We took 4 g of the bromides, 6 g of zinc dust, and 15 ml of pyridine. The reaction lasted 6 hours. The acid yield was 2.03 g (79.61%, based on the oleic acid, $C_{18}H_{34}O_2$). The debromination product was not saponified, nor was the molecular weight determined; rebromination and debromination were undertaken.

Found: iodine number 118.56, 118.00.

Bromination of the debromination product. We took 1.6 g of the acid and 40 ml of petroleum ether. The bromide yield was as follows: 1) solid, insoluble in petroleum ether, 0.45 g (28.13%); 2) liquid, soluble in petroleum ether, 2.41 g (150.62%).

Per cent bromine in solid bromides: Found 56.77, 56.43.

Though the per cent bromine is not high in this case, there is no reason to regard these bromides as derivatives of linoleic and linolenic acids: in view of their fusion behavior and their behavior toward solvents, they are more likely to be derivatives of highly unsaturated acids.

Per cent bromine in the liquid bromides: Found 42.20, 42.12.

Redebromination of the liquid bromides obtained by brominating the crude oleic acid secured from the Fraction VI bromides. 1.40 g of the bromides, 3 g of zinc dust, and 9 ml of pyridine. The acid yield was 0.70 g (78.65%, based on oleic acid). The resultant acid was brominated in 20 ml of petroleum ether. No solid bromides were collected because of their minute quantity. The yield of liquid bromides totaled 0.9 g (128.6%, based on oleic acid).

Per cent bromine in the liquid bromides: Found 37.21, 36.90. $C_{18}H_{34}O_2Br_2$. Calculated %: Br 36.18.

It may therefore be regarded as proven that the Fraction VI bromides are derivatives of oleic acid. The original bromine percentage in this Fraction VI is excessively high because of the presence in the solution of solid bromides of highly unsaturated acids, which are more or less completely crystallized out of the liquid bromides only after successive bromination and debromination. The more slowly the drops of bromine are added to the solution of the acid in petroleum ether, the more completely the solid bromides crystallize out of the liquid bromides.

Composition of the Oil in the Liver of Perca schrenki

The constants of this oil are given in Table 1. All the benzene fractions of the bromides obtained from the acids in the oil of the liver are derivatives of highly unsaturated acids. The per cent bromine in the bromides obtained from the acids in the oil is given in Table 6.

TABLE 6

Per cent Bromine in Bromides Obtained from the Acids in the Oil of the Liver of Perca schrenki

Bromide fraction	% Yield of bromides	% Bromine
I	21.0	70.65, 70.46
II	2.3	70.55, 70.30
III	7.50	66.40, 66.26
VI	92.0	41.00, 41.11

Table 6 indicates that the per cent bromine in the Fraction I and II bromides is equivalent to clupanodonyl decabromide, $C_{22}H_{34}O_2Br_{10}$. Thus the liver of the Balkhash perch is the only tissue whose oil contains clupanodonic acid as typical of the highly unsaturated acids. Terapinic acid is most typical of the highly unsaturated acids in the oils of all the other tissues of the Balkhash perch. The per cent bromine in the Fraction I mides of the acids in the liver oil of the Balkhash perch indicates that it has the most highly unsaturated acids of all the tissue of Perca schrenki that we have analyzed, whereas a different picture is obtained in the case of the river perch [10]: the Fraction I bromides of the acids in the liver oil of Perca fluviatilis contain a lower percentage of bromine than the same fraction of all the other tissues of that species.

TABLE 7

Per Cent Bromine in the Bromides Obtained from the Acids in the Oil of the Roe of Perca schrenki

Bromide fraction	% Yield of bromides	% Bromine
I	17.06	69.56, 69.51
II	3.27	68.89, 68.65
III	8.26	67.07, 67.21
V	2.10	67.70, 67.58
VI	102.2	40.26, 40.10

Composition of the Oil in the Roe of Perca schrenki

The constants of the roe oil are given in Table 1; the per cent bromine in the bromides of the acids in the oil of the roe of the Balkhash perch is given in Table 7.

Terapinic acid from the Fraction I bromides. We took 3.5 g of the bromides, 7 g of zinc dust, and 15 ml of pyridine. The acid yield was 0.97 g (91.51%, based on terapinic acid). The acid was brominated in 40 ml of ether. The bromide yield was as follows: 1) insoluble 1.39 g (143.3%); 2) soluble 1.22 g (125.77%). The m.p. of the soluble bromides was 94-95°.

Per cent bromine in the insoluble bromides: Found 69.70, 69.57. $C_{18}H_{28}O_2Br_6$. Calculated %: Br 69.83.

Per cent bromine in the soluble bromides: Found 67.29, 67.24.

Redebromination. We took 1.13 g of the bromides, 3 g of zinc dust, and 8 ml of pyridine. The acid yield was 0.31 g (91.18% of the theoretical, based on terapinic acid). The acid was brominated in 20 ml of ether. The bromide yield was as follows: 1) insoluble 0.35 g (112.90%); 2) soluble 0.43 g (138.7%). The m.p. of the soluble bromides was 89-90°.

Per cent bromine in the insoluble bromides: Found 68.36, 68.52.

The per cent bromine was one whole per cent lower than in the initial bromides of the first debromination and bromination of that Fraction I. It should be noted that the polybromides of the acids of the roe oil and the roe oil acids themselves are particularly unstable, compared to the bromides and acids of the oils in other tissues of the fish.

Per cent bromine in the soluble bromides: Found 36.30, 66.34. The per cent bromine in the soluble bromides is likewise lower than in the soluble bromides of the initial bromination of the debromination product.

Arachidonic acid from the Fraction III bromides. 1.70 g of the bromides, 3 g of zinc dust, and 9 ml of pyridine. The acid yield was 0.48 g (87.27% of the theoretical, based on arachidonic acid). The acid was brominated in 20 ml of ether. The bromide yield was as follows: 1) insoluble 0.47 g (88.7%); 2) soluble 0.84 g (158.3%). The m.p. of the soluble bromides was 90-91°.

Per cent bromine in the insoluble bromides: Found 68.21, 68.17.

We see that the per cent bromine is higher than that in the Fraction III bromides prior to debromination.

Per cent bromine in the soluble bromides: Found 64.52, 64.44.

Oleic acid from the Fraction VI bromides. We took 3 g of the bromides, 7 g of zinc dust, and 10 ml of pyridine. The acid yield was 1.50 g (78.54%, based on oleic acid). The debromination product was not saponified.

Found: iodine number 103.30, 102.25.

Bromination of the crude oleic acid. 1.20 g of the acid was dissolved in 30 ml of petroleum ether; after the turbidity had been filtered out, the solution brominated in the usual manner. The bromide yield wasas follows: 1) solid 0.19 g (15.83%); 2) liquid 1.83 g (152.52%).

Per cent bromine in the solid bromides: Found 56.90, 56.80.

Per cent bromine in the liquid bromides: Found 38.60, 38.35.

TABLE 8

Per Cent Bromine in the Bromides Obtained from the Acids in the Oil of the Roe of Perca fluviatilis

Bromine Number	% Yield of bromides	% Bromine
I	20.0	70.50, 70.40
II	4.86	69.55, 69.41
III	10.88	67.20, 67.09
V	3.33	66.02, 66.19
VI	92.70	39.25, 38.90
VIII	3.33	51.29, 51.17

Acid Composition of the Oil of the Roe of Perca fluviatilis

We seized an opportunity to recover material on the acid composition of the oil of the roe of the river perch Perca fluviatilis L. The accumulation of the material (oil), the preparation of the bromides, and all the other processing were effected under the conditions described.

The per cent bromine in the bromides obtained from the acids of the roe oil of the river perch is given in Table 8.

Clupanodonic acid from the Fraction I bromides. We took 9.32 g of the bromides, 8 g of zinc dust, and 40 ml of pyridine, the reaction lasting 8 hours. The acid yield was 2.77 g (84.0% of the theoretical, based on clupanodonic acid).

Found: iodine number 367.80, 368.90; M 379.25.

Bromination of the crude clupanodonic acid. 1.20 g of the acid was dissolved in 50 ml of ether and brominated in the usual manner. The bromide yield was as follows: 1) insoluble 1.95 g (162.5%); 2) soluble 1.82 g (141.67%). The m.p. of the soluble bromides was 61-62°.

Per cent bromine in the insoluble bromides: Found 70.68, 70.50. $C_{22}H_{34}O_2Br_{10}$. Calculated %: Br 70.75.

It is quite apparent that clupanodonic acid is present.

Per cent bromine in the soluble bromides: Found 67.60, 67.48.

Terapinic acid from the Fraction II bromides. 1.75 g of the bromides, 5 g of zinc dust, and 10 ml of pyridine. The acid yield was 0.48 g (94.14%, based on terapinic acid). The acid was dissolved in 20 ml of ether and brominated, the bromide yield being as follows: 1) insoluble 0.60 g (125.0%); 2) soluble 0.80 g (166.6%). The m.p. of the soluble bromides was 54-55°.

Per cent bromine in the insoluble bromides: Found 69.23, 69.30. $C_{18}H_{32}O_2Br_8$. Calculated %: Br 69.83.

Per cent bromine in the soluble bromides: Found 65.61, 65.75

Arachidonic acid from the Fraction III bromides. We took 5.40 g of the bromides, 9 g of zinc dust, and 20 ml of pyridine. The yield totaled 1.65 g (94.82%, based on arachidonic acid).

Found: iodine number 334.21, 334.30.

Bromination of the crude arachidonic acid. We took 0.70 g of the acid and dissolved it in 20 ml of diethyl ether. The bromide yield was as follows: 1) insoluble 0.82 g (117.14%); 2) soluble 1.15 g (164.3%). The m.p. of the soluble bromides was 51-52°.

Per cent bromine in the insoluble bromides: Found 67.21, 67.10. $C_{20}H_{32}O_2Br_8$. Calculated %: Br 67.75.

Per cent bromine in the soluble bromides: Found 65.51, 65.66.

Oleic acid from the Fraction VI bromides. We took 15.83 g of the bromides, 15 g of zinc dust, and 50 ml of pyridine. The reaction lasted 8 hours. The acid yield was 8.0 g (79.20% of the theoretical, based on oleic acid). The entire debromination product was saponified with 100 ml of a 0.5 N alcoholic solution of KOH in the usual manner. The acid yield after saponification was 7.37 g.

Found: iodine number 96.21, 96.12.

Bromination of the crude oleic acid. 6.50 g of the acid was dissolved in 65 ml of petroleum ether, the solution was filtered, and the filtrate brominated. The bromide yield was as follows: 1) solid 1.20 g (18.46%); 2) liquid 7.24 g (111.4%).

Per cent bromine in the solid bromides: Found 61.49, 61.30.

Per cent bromine in the liquid bromides: Found 37.08, 37.12.

Oleic acid from the redebromination of the Fraction VI liquid bromides. We took 6.60 g of the bromides, 10 g of zinc dust, and 20 ml of pyridine. The yield of oleic acid was 3.30 g (37.20% of the theoretical).

Found: iodine number 90.01, 90.30.

Rebromination of the oleic acid. 1.65 g of the acid was dissolved in 20 ml of petroleum ether and brominated in the usual manner. The bromide yield consisted of 2.21 g of liquid bromides (133.93%). No solid bromides were collected because of their minute quantity.

Per cent bromine in the liquid bromides: Found 36.21, 36.30. $C_{18}H_{34}O_2Br_2$. Calculated %: Br 36.18.

These findings are further incontrovertible proof of the previous conclusion that the Fraction VI bromides are derivatives of oleic acid.

SUMMARY

1. The oils in all the tested parts of the carcass and tissues of the Balkhash perch Perca schrenki contain highly unsaturated acids with four or five double bonds, which is a characteristic of the oil of Perca schrenki, as of all fish oils.

2. The acid composition of the oil of the carcass, the head, the viscera, and the roe is almost identical, while the acid composition of the liver oil exhibits a higher degree of unsaturation of its highly unsaturated acids.

3. The most typical of the highly unsaturated acids of the oil in all the tissues, with the exception of the liver, is terapinic acid with four double bonds, $C_{18}H_{32}O_2$ (up to 15%). The tissue oils of Perca schrenki contain a smaller percentage of another acid of the same series: arachidonic acid, $C_{20}H_{32}O_2$ (up to 5%).

4. Clupadonic acid $C_{22}H_{32}O_2$, with five double bonds, (up to 15%) is the typical highly unsaturated acid of the liver oil of Perca schrenki; in this respect the acid composition of the liver oil of Perca schrenki closely resembles the acid composition of the oil in all the tissues of Perca fluviatilis.

5. The highest percentage of the acids comprising the oil of Perca schrenki is constituted by oleic acid.

6. The lower degree of unsaturation of the highly unsaturated acids in the oils in all the tissues of Perca schrenki, with the sole exception of the liver, than exists in the highly unsaturated acids of the oils in the corresponding tissues of Perca fluviatilis is due to the influence of the external living conditions of the fish upon the constitution of its oils.

7. The most active constituents of the oils of fresh-water fish are the highly unsaturated acids, which are transformed in accordance with the changes in the conditions governing their formation more rapidly than any other constituent of the oil. The most stable of the unsaturated acids is oleic acid.

8. The usual unsaturated acids, linoleic and linolenic acids, are not present in the oils of any of the tested tissues and parts of Perca schrenki.

9. No liquid bromides are produced during the rebromination of the crude acids produced from the benzene fractions of bromides, though approximately equal parts of bromides soluble in diethyl ether and insoluble bromides are always produced.

10. The less bromine there is present in the bromide molecule, the harder it is to split off the bromine with zinc in a pyridine solution and the lower the acid yield.

11. The (liquid) Fraction VI bromides dissolve a certain amount of the solid bromides of the benzene fractions, which explains their initial excessively high bromine content. The solid bromides crystallize out of the liquid bromides completely during repeated alternating debromination and bromination, yielding the pure dibromide as a derivative of oleic acid.

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THE ELECTROLYTIC REDUCTION OF LEPIDINES

I. THE ELECTROLYTIC REDUCTION OF LEPIDINE IN AN ACID MEDIUM

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We know [1] that reducing lepidine chemically by boiling it with hydrochloric acid and tin in an acid medium yields tetrahydrolepidine, while reducing lepidine in an alkaline medium [2] (reacting it with sodium amalgam containing 10% sodium) yields a yellowish oil as a product, which when boiled with dilute nitric acid yields a red crystalline substance, $C_{20}H_{18}N_2 \cdot HNO_3$, called dilepidine nitrate.

No one has yet reduced lepidine electrolytically. We undertook the present research to determine the feasibility of reducing lepidine electrolytically, as compared with quinoline [3] and quinaldine [4].

When we reduced lepidine electrolytically in an acid medium, we not only identified tetrahydrolepidine, which is also produced by the chemical reduction of lepidine, but also found a new product, dihydrolepidine, corresponding to dihydroquinoline [3] and dihydroquinaldine [4].

The lepidine was reduced electrolytically in sulfuric acid. We investigated the influence of voltage, current density, electrolysis time, temperature, and acid concentration. We found that a new crystalline product with a m.p. of 279° is obtained under certain conditions.

The maximum product yield (7.62% of the theoretical) is secured at a flowing mercury cathode [6] at a C.D. of 38 amps/sq dm, electrolysis time of 60 minutes, and a temperature of +18°. This product does not dissolve in alkalies, while in acids it dissolves only when heated in conc. hydrochloric acid. When the solution is neutralized with alkali, it is precipitated unchanged. It is sparingly soluble in the cold in chloroform, benzene, toluene, xylene, and glacial acetic acid; when heated in these solvents, it dissolves freely, but is precipitated in crystalline form when the solutions cool. Its crystals from toluene have the shape of prisms with beveled edges. The synthesized product does not color a solution of potassium dichromate in sulfuric acid, though tetrahydrolepidine does. Its elementary analysis indicated that its composition was $C_{19}H_{11}N$. Its molecular weight, by the Rast method, is 288.1. This shows that this product is a dimer of dihydrolepidine $(C_{10}H_{11}N)_2$. When reacted with picric acid, the product yields a picrate as acicular crystals. Picrate m.p. 222-223°. The elementary analysis of the picrate furnished corroboration of the assumption that the product is a dimer of dihydrolepidine.

When we reduced lepidine chemically in a hydrochloric solution with tin, we did not obtain the product we secured in the electrolytic reduction of lepidine.

EXPERIMENTAL

Electrolytic reduction of lepidine in acid. 3 ml of lepidine (3.24 g) was dissolved in 47 ml of a 10% solution of sulfuric acid. The prepared solution was placed in the cathode chamber and served as the catholyte. Mercury was used as the cathode. The anode chamber was a cylindrical glass vessel, separated from the cathode chamber by two sheets of cellophane. A 10% solution of sulfuric acid (20 ml) was poured into the vessel. Platinum was used as the anode. A layer of ether (20 ml) was poured over the surface of the catholyte to prevent foaming during electrolysis. After several experiments we chose a C.D. of 38 amps/sq.dm at a voltage of 10-11 volts. Cooling was employed to keep the temperature of the electrolyte from rising above 18° throughout electrolysis. Electrolysis lasted 60 minutes.

Isolation of the reaction product. Ten electrolysis runs were made, 32.4 g of lepidine undergoing electrolytic reduction. At the end of one hour, the catholyte, which was a transparent orange solution, was poured into a separatory funnel to remove the layer of ether, which was a faint yellow. All the acid catholytes of the ten runs were combined and diluted with water to make 1 liter for the wash waters of the electrolyzer. The dark-green resinous product deposited on the surface of the mercury cathode after electrolysis was carefully removed in every case and analyzed separately.

Processing of the ether layer. The ether was driven off on a water bath, a yellow resinous product that contained a white crystalline deposit settling on the wall of the flask. These products totaled 1.2 g (3.65%). The resinous substance was washed away in the cold with benzene. The remaining crystalline deposit was dissolved in boiling benzene. As the benzene solution cooled, a yellowish crystalline deposit settled out (0.3% yield), which was filtered out, dried, and recrystallized from boiling benzene. This yielded a white crystalline product with a m.p. of 279°.

Processing the catholyte. After the catholyte had been diluted with water, it was treated with alkali (an 18% solution of potassium hydroxide) until its reaction was alkaline. A milky emulsion was formed, with a small quantity of a faintly green oily product separating out on top. The alkaline solution was distilled with steam to remove the unchanged lepidine and the volatile tetrahydrolepidine. Distillation was continued until a sample of the distillate no longer colored a solution of potassium dichromate in sulfuric acid red (test for tetrahydrolepidine). The distillate was an oily product, which was extracted with ether. The ether extract was dried over anhydrous sodium sulfate, and the ether was driven off. This yielded a yellowish oil, consisting of unreacted lepidine with some tetrahydrolepidine. 8.1 g of this mixture (25%) was obtained. After the steam distillation, the distillation flask contained a yellow-green resinous residue, which solidified into a brittle mass upon being dried. This mass was pulverized and processed with ether. The ether dissolved the resinous substance, the insoluble crystalline residue being filtered out and dried; it weighed 0.4 g (1.22%). Repeated recrystallization from boiling toluene yielded a white crystalline product with a m.p. of 279°.

Processing the product deposited on the cathode. After the resinous product deposited on the cathode had been dried, it weighed 4.5 g (13.9%). It was treated with ethyl alcohol, the insoluble portion being a faintly yellow crystalline precipitate. This crystalline product was filtered out and dried; it weighed 0.7 g (2.13%). Repeated recrystallization from boiling toluene yielded white crystals with a m.p. of 279°. Their mixed m.p. with the crystalline products secured from the ether and aqueous parts of the catholyte and from the cathode deposit exhibited no depression, and they all proved to have wholly identical physical and chemical properties. The overall yield of the crude product totaled 1.2 g (3.65%).

2.625 mg subs.: 7.980 mg CO_2; 1.787 mg H_2O. 3.027 mg subs.: 9.189 mg CO_2; 2.089 mg H_2O. Found %: C 82.96, 82.84; H 7.60, 7.71. $(C_{10}H_{11}N)_2$. Calculated %: C 82.71; H 7.64. 5.312 mg subs.: 0.459 ml N_2 (19°, 740 mm). 4.384 mg subs.: 0.376 ml N_2 (20°, 743 mm). Found %: N 9.83, 9.77. $(C_{10}H_{11}N)_2$. Calculated %: N 9.65. 0.0058 g subs.: 0.0781 g camphor: Δt 10.5°. 0.0029 g subs.: 0.0639 g camphor: Δt 6.3°. Found: M 282.9, 288.1 $(C_{10}H_{11}N)_2$. Calculated M 290.4.

The foregoing indicates that the product is a dimer of dihydrolepidine. This is also indicated by the analysis of the picrate.

3.489 mg subs.: 0.413 ml N_2 (19°, 742.4 mm). 4.370 mg subs.: 0.512 ml N_2 (19°, 742.4 mm). Found %: N 13.63, 13.39. $(C_{10}H_{11}N)_2 \cdot C_6H_2(OH)(NO_2)_3$. Calculated %: N 13.48.

The variation of the product yield in the reduction of lepidine with the manner (rate) of renewing the mercury at a C.D. of 38 amps/sq.dm, an electrolysis time of 60 minutes, and a temperature of 18° is given in the following table (the average of 10 experiments in each instance):

Cathode	Yield of crystalline product with a m.p. of 279° (% of the theoretical)
Unrenewable mercury cathode	3.65
Renewable mercury cathode	5.18
Flowing mercury cathode	7.62

SUMMARY

1. It has been shown that the electrolytic reduction of lepidine at a mercury cathode in an acid medium results in the production of a new crystalline product, in addition to the tetrahydrolepidine which is produced in chemical methods of reduction.

2. It has been proved that this product is a dimer of dihydrolepidine.

3. It has been established that the yield of the dimer is a maximum at a renewable flowing mercury cathode.

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A STUDY OF THE SIDE REACTIONS IN THE CONTACT SYNTHESIS OF DIVINYL FROM ALCOHOL BY THE S. V. LEBEDEV METHOD

II. THE FORMATION OF COMPOUNDS WITH AN ODD NUMBER OF CARBON ATOMS (C_1 and C_3)

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In our preceding paper [1], we discussed the formation of side products in the S. V. Lebedev reaction that had an even number of carbon atoms. The manner in which compounds possessing an odd number of carbon atoms are produced is of considerable interest.

S. V. Lebedev [2] considered the principal reason for the occurrence of the odd-numbered forms to be the decomposition of molecules of the even-numbered series. He attributed the formation of carbon monoxide and methane to the decomposition of acetaldehyde. Another source of the origin of the odd-numbered forms, according to S. V. Lebedev, could be formaldehyde, produced by the reaction of carbon monoxide with hydrogen in statu nascendi, which is present in high concentration in the reaction sphere. The ensuing addition of one molecule of formaldehyde to even-numbered molecules could result in formation of the odd-numbered forms.

We shall not dwell on the diagrams advanced by S. V. Lebedev for the reactions involved in the formation of odd-numbered products, referring the reader to his paper [2]. We merely want to point out that these suggestions were of considerable importance for the subsequent research on the manner in which odd-numbered by-products are formed. It should be stated that the experimental underpinning for the way in which all the odd-numbered by-products are formed has not been fully laid down as yet, though several actually corroborated schemas can already be set forth for most of them.

In the present paper we shall confine ourselves to discussing the problems involved in compounds containing 1 and 3 carbon atoms. We dealt with the formation of C_5 and C_7 compounds in our previous papers [20, 21].

C_1 group. We demonstrated the origin of carbon monoxide and methane in the decomposition of acetaldehyde, as conjectured by S. V. Lebedev, by passing acetaldehyde over a binary catalyst [3] as well as over its separate components [4]. The reaction gas was found to contain as much as 65% of carbon monoxide and methane. The formation of CO_2 may be due either to the production of ethyl acetate, which is then hydrolyzed, with the resulting acetic acid breaking down, or to a double oxidation-reduction of two particles of acetaldehyde with water, yielding acetic acid, which is decomposed to CO_2. This reaction will be discussed at length below.

C_3 group. Propylene and acetone, among the substances in this group, have been found in the products of the S. V. Lebedev reaction. In order to test the manner in which propylene is formed via aldol as conjectured by S. V. Lebedev, one of the present authors together with E. I. Silinskaya in 1935 ran experiments on the decomposition of aldol at 450° over a dehydrating component of a catalyst. We found that the gaseous conversion products contained high percentages of carbon monoxide and propylene, while crotonaldehyde was found in the liquid products. The figures on the composition of the gas in these tests are given in Table 1.

The reaction may be represented as follows:

Schema 1

1. $CH_3-CHOH-CH_2-CHO \longrightarrow H_2O + CH_3-CH=CH-CHO$

2. $CH_3-CH=CH-CHO \longrightarrow CH_3-CH=CH_2 + CO.$

Thus the conjecture of S. V. Lebedev's has been confirmed experimentally.

We made no attempt to secure experimental verification of the possibility of producing acetone from aldol by splitting off carbon monoxide and then dehydrogenating the resultant isopropyl alcohol with the dehydrogenating component of the catalyst (or by first dehydrogenating the alcohol group of the aldol and then splitting off the carbon

TABLE 1

Composition of the Gaseous Products Formed in the Decomposition of Aldol Over the Dehydrating Component of a Catalyst at 450° (Fractional Distillation Into a Tower of the Podbilnyak Type)

Constituents of the gas	Vol. %
Carbon monoxide	32.6
Hydrogen	15.2
Methane	3.8
Ethylene	16.6
Propylene	21.1
C_4 hydrocarbons	7.4
Residue	3.3

monoxide). This manner of producing acetone seems rather unlikely, however, for the following reasons: both the temperature at which carbon monoxide is split out of aldehydes and the temperature of the catalytic dehydrogenation of alcohols are much higher than the upper temperature limit of the stability of aldol, at which water is split out of the aldol (80-90°). Thermodynamic calculations by B. N. Dolgov and V. V. Mazurek have shown that it is unlikely that carbon monoxide is split out of aldol [5]. We also know the readiness with which secondary alcohols undergo catalytic dehydration; so that we think the first stage must involve the splitting out of elements of water from aldol rather than carbon monoxide, and the formation of crotonaldehyde rather than isopropyl alcohol. Nonetheless, we cannot abandon the formation of acetone via aldol entirely. The references in the literature—the papers by Komarewsky and his collaborator [6]—indicate that such reactions are possible when a dehydrogenating catalyst is employed. These authors passed propyl, butyl and other primary alcohols over chromic oxide at 350-450° and secured the corresponding symmetrical ketones; they conjectured that the reaction involved the dehydrogenation of the alcohols to aldehydes and the latter's condensation to aldols, followed by the splitting out of carbon monoxide and the formation of ketones. The same viewpoint was set forth even earlier by V. N. Ipatyev and N. A. Kiyukvin [7]. Still, it seems to us that aldol decomposition is not the sole possible channel for the formation of acetone in the S. V. Lebedev process. Several references in the literature and our own experimental findings indicate that acetone can be produced in another way.

Goldschmidt, Askenasy, and Grimm [8] showed that acetic acid and some ethyl alcohol are produced when a mixture of acetaldehyde and steam is passed over various catalysts with atmospheric oxygen excluded. Ya. M. Slobodin and F. Yu. Rachinsky [9] passed acetaldehyde over alumina gel (Al_2O_3), floridin, and a Cu-Mg mixture at 250-300-400° and secured ethyl acetate and acetic acid as a reaction by-product; the same authors passed ethyl acetate over a S. V. Lebedev catalyst at high temperature and found divinyl (11.5% by volume) in the gaseous reaction products. These researches have demonstrated that acetic acid and alcohol can be produced catalytically from acetaldehyde.

According to Sabatier and Mailhe [10] and Ipatyev [11], the catalytic decomposition of ethyl acetate at high temperature over oxides of some divalent metals results in the formation of acetone, carbon dioxide, ethylene, and water.

Ethyl acetate is converted into acetone by first saponifying it to alcohol and acetic acid. Both Ipatyev [11,12] and Senderens [13] have found that when the latter is decomposed over barium, calcium and aluminum oxides, it readily undergoes ketonic cleavage and is converted into acetone. As M. Ya. Kagan has shown, acetone can be produced from alcohol over catalysts that consist of mixtures of ferric oxide with oxides of the alkali-earth metals [14]. It is conjectured that the intermediate reaction product is ethyl acetate, which then decomposes to yield acetone.

It has been previously established that about 2% of acetone is produced from ethyl alcohol over the dehydrating constituent of the S. V. Lebedev catalyst [4].

We also know that the products of the catalytic conversion of ethyl alcohol to divinyl by the S. V. Lebedev process contain ethyl acetate as a reaction by-product [1].

The research results described in the experimental part of the present paper indicated that acetic acid is nearly entirely decomposed at high temperatures over a S. V. Lebedev catalyst, being converted into carbon dioxide and acetone. Under these same conditions ethyl acetate yields acetone, carbon dioxide, propylene, ethylene, some divinyl, and water, in addition to other products. In the research we undertook in collaboration with D. S. Novikova [4] we found that a small quantity of acetone is produced in the decomposition of acetaldehyde over the dehydrogenating constituent of the catalyst. As the experimental temperature is raised from 300 to 450°, the acetone yield rises from 0.2% to 1.0%. The gaseous reaction products still contain high percentages of carbon dioxide, hydrogen, carbon monoxide, methane, plus a small percentage of ethylene. The yield of acetone over the dehydrating component of the catalyst is lower than over the dehydrogenating component. It totaled 0.40% at 450°, the percentage of ethylene being nearly ten times higher than over the dehydrogenating catalyst, while the hydrogen yield is much lower.

Thus, under the specified conditions acetaldehyde yields compounds that greatly resemble the products of the decomposition of ethyl acetate and acetic acid, in addition to the decomposition products: carbon monoxide and

methane. It is probable that in this instance the acetaldehyde is partially converted into alcohol and acetic acid by double oxidation-reduction. This conversion may be a Cannizzaro reaction [15] or a V. E. Tishchenko reaction [16], involving an ester condensation of the aldehyde, followed by saponification of the ester to ethyl alcohol and acetic acid. Under the prevailing reaction conditions acetic acid is converted into acetone and carbon dioxide. The ethyl alcohol is decomposed either into ethylene and water or into the aldehyde and hydrogen, depending on the catalyst component over which the reaction takes place. It seems to us that the experimental data justifies the adoption of the following pattern of formation of acetone in the S. V. Lebedev process, paralleling the production of acetone via aldol.

Schema 2

1. $2CH_3{-}COH + H_2O \rightarrow CH_3COOH + CH_3CH_2OH$ (or $2CH_3CHO \rightarrow CH_3COOC_2H_5 \xrightarrow{+HOH} CH_3COOH + CH_3CH_2OH$)
2. $2CH_3COOH \longrightarrow CH_3{-}CO{-}CH_3 + CO_2 + H_2O$.

The decomposition of acetic acid as outlined above may explain the presence of CO_2 in the gases of the catalytic conversion of alcohol to divinyl [17]. Furthermore, one of the present authors and F. N. Kogan [18] have shown that adding acetone to alcohol during the catalytic conversion of the latter into divinyl increases the percentage of propylene in the reaction gases as a result of the acetone being reduced by the ethyl alcohol to isopropyl alcohol, which gives off elements of water under the influence of the dehydrating component of the catalyst and is converted into propylene. We have shown that when ethyl acetate is passed over the S. V. Lebedev catalyst at high enough temperatures a substantial quantity of propylene is produced in addition to some acetone and other products. Evidently, under the S. V. Lebedev reaction conditions the alcohol produced during saponification of the ester converts the acetone into propylene as indicated above.

It seems that the formation of propylene in the S. V. Lebedev process may be described not only by Schema 1 (vide supra), but also by what we consider to be the more probable Schema 3, which is a development of Schema 2.

Schema 3

3. $CH_3{-}CO{-}CH_3 + 2H \longrightarrow CH_3{-}CHOH{-}CH_3$.
4. $CH_3{-}CHOH{-}CH_3 \longrightarrow H_2O + CH_3{-}CH{=}CH_2$.

In the present research, in addition to studying the decomposition of acetic acid and ethyl acetate, we investigated the conversion of binary mixtures of each of these substances with ethyl alcohol, using various percentages of the latter, over the S. V. Lebedev catalyst. In the catalytic decomposition of a mixture of acetic acid and ethyl alcohol (Table 2), the percentages of carbon dioxide and propylene increase with an increase in the percentage of acetic acid in the original mixture, while the percentages of divinyl and hydrogen fall. The per cent ethylene rises at first, reaches a maximum, and then drops off. The percentage of acetone in the liquid reaction products increases, starting with the mixture containing 10% of acetic acid; the percentage of the aldehyde in the condensate rises at first, but then drops off. Ethyl acetate was found in the runs in which an equimolar mixture of alcohol and acetic acid was employed. Thus, the ethyl alcohol is partially esterified in the reaction conditions. The divinyl yield, based on the alcohol throughput and on the reacted alcohol, drops off as the percentage of acetic acid in the original mixture is raised (Table 3), the percentage of decomposed alcohol falling at the same time. The yield of ethylene, based on the decomposed alcohol, rises with increasing concentration of acetic acid in the original mixture. The ethylene yield remains practically unchanged in terms of the alcohol throughput. In the runs using pure acetic acid the gas consisted almost entirely of carbon dioxide with a little unsaturated hydrocarbons and hydrogen. More than half of the condensate consisted of acetone in these runs, the acetone yield being over 70% of the theoretical. Thus, acetic acid undergoes ketonic cleavage as outlined in Schema 2 (vide supra) over an S. V. Lebedev catalyst, carbon dioxide being evolved. In the conditions prevailing during these runs the acetic acid is decomposed almost completely, an indication of its instability, as well as of the fact that its adsorption on the catalyst is higher than that of ethyl alcohol. This is probably why the percentage of reacted alcohol decreases as the percentage of acetic acid in the original mixture is raised.

The increase in the per cent ethylene in the gas and the rise in its yield, based on the reacted alcohol, on the one hand, and the decrease in the production of hydrogen and the increase in the per cent aldehyde in the condensate, on the other, indicate that the dehydrogenating and dehydrating components of the catalyst act differently upon the acetic acid. The dehydrogenation of the alcohol to the aldehyde and the condensation of the alcohol, which take place over the dehydrogenating component of the catalyst, are suppressed, which may be attributed to the predominant adsorption of acetic acid at this component. On the other hand, the dehydration of the alcohol and the production of ethylene increase.

The suppression of the reactions involved in the formation of the aldehyde and its condensation are why the yield of divinyl drops, based on the reacted alcohol. The rise in the percentage of propylene in the gas is attributed

TABLE 2

Contact Conversion of an Alcohol-Acetic Acid Mixture and of Acetic Acid Alone Over an S. V. Lebedev Catalyst at 380°

Run No.	Acetic acid in alcohol mixture (wt.%)	Mixture used (g)	Yield		Composition of condensate, wt. %						Composition of gas, volume %					
			Condensate, (g)	Gas at standard conditions, deducting air	Alcohol	Acetic acid	Acetone	Acetaldehyde	Water-insoluble compounds	Ethyl acetate	CO_2	CO	H_2	C_2H_4	$C_3H_6 + C_4H_8$	C_4H_6
1	0	113.3	84.8	19.95	62.4	None	Traces	1.0	0.6	Not determined	1.5	1.2	49.9	7.8	4.9	35.2
2	0	113.3	80.8	22.4	61.2	None	Traces	0.9	0.4		1.4	1.1	49.0	7.9	4.8	34.5
3	0	113.3	80.9	23.1	59.0	None	Traces	0.85	0.7		0.8	1.1	46.7	9.2	4.8	35.8
4	1	80.9	60.1	14.2	61.6	None	Traces	1.2	—	"	1.6	1.1	46.7	10.8	5.5	34.9
5	1	80.9	59.7	14.2	62.0	None	Traces	1.1	—	"	1.1	0.6	46.0	10.6	5.4	34.9
6	5	123	102.4	13.0	68.7	0.06	Traces	1.3	0.5	"	4.3	0.8	40.4	15.5	5.1	31.5
7	5	123	100.1	11.7	69.3	0.09	Traces	1.6	0.5	"	3.7	0.6	37.9	17.5	5.6	34.6
8	10	82.7	66.6	8.3	66.3	0.13	0.33	2.5	0.4	"	12.2	0.9	26.6	21.0	9.3	27.6
9	10	124	106.5	8.8	68.7	0.57	0.42	2.9	0.4	"	11.7	0.5	26.5	25.3	7.2	25.4
10	55.2	140	102.4	17.5	39.8	1.36	21.0	0.1	Traces	8.9	73.3	0	4.0	5.0	9.6	5.1
11	55.2	140	98.8	16.6	43.6	1.58	20.0	0.1	0.2	10.1	73.8	0	3.7	5.8	10.4	4.5
12	55.2	140	103.2	15.8	39.9	1.90	19.2	0.1	0.45	11.85	72.0	0	4.1	7.7	9.6	4.4
13	100	105.1	52.6	20.4	—	0.18	62.0	—	0.9	—	92.0	0	1.5	—	4.4	—
14	100	105.1	51.8	20.6	—	0.30	55.6	—	0.9	—	94.6	0	1.6	—	2.1	—

TABLE 3

Yield of Reaction Products in Tests of the Decomposition of Alcohol–Acetic Acid Mixtures and of Acetic Acid Alone over an S.V.Lebedev Catalyst

Run No.	Acetic acid in alcohol mixture, weight %	C_4H_6 yield, wt. % based on alcohol		C_2H_5 yield, wt. % based on alcohol		Yield			Per cent	
		Throughput	Reacted	Throughput	Reacted	Acetone, wt.% based on decomposed acetic acid	% Ethyl acetate, based on decomposed alcohol and acetic acid	Acetone, % of the theoretical	Decomposed alcohol as a percentage of the throughput	Decomposed acetic acid as a percentage of throughput
1	0	16.5	33.0	1.8	3.7	Traces	—	—	50	—
2	0	18.1	34.1	2.1	3.9	Traces	—	—	53	—
3	0	19.4	35.5	2.5	4.6	Traces	—	—	54.8	—
4	1	16.3	32.8	2.0	5.0	Traces	—	—	50.7	100
5	1	16.3	32.2	2.5	4.9	Traces	—	—	50.7	100
6	5	9.2	25.7	2.3	6.5	Traces	—	—	35.7	99
7	5	9.2	26.0	2.3	6.6	Traces	—	—	35.4	95.7
8	10	7.9	21.7	3.2	8.7	3.0	—	—	36.5	99
9	10	5.2	17.5	2.6	8.8	3.7	—	—	30.0	98.5
10	55.2	3.6	11.6	2.0	8.8	32.4	9.7	—	30.8	98.2
11	55.2	3.3	12.2	2.2	8.2	29.3	10.8	—	27.0	98.1
12	55.2	2.8	9.54	2.8	9.5	28.7	13.1	—	30.0	97.5
13	100	—	—	—	—	37.3	—	77.4	—	100
14	100	—	—	—	—	33.3	—	68.9	—	100

TABLE 4

Contact Conversion of an Alcohol–Ethyl Acetate Mixture and of Ethyl Acetate Alone over an S.V.Lebedev Catalyst at 380°

Run No.	Ethyl acetate in alcohol mixture, wt.%	Mixture used, g	Yield: Condensate, g	Yield: Gas at standard conditions, deducting air	Composition of condensate, wt. %: Alcohol	Acetic acid	Acetone	Acetaldehyde	Water-soluble compounds	Ethyl	Composition of gas, volume %: CO_2	CO	H_2	C_2H_4	C_3H_6 + C_4H_8	C_4H_6
1	0	113.3	84.7	18.95	62.4	–	None	Traces	1.0	0.6	1.5	1.5	49.9	7.8	4.9	35.2
2	0	113.3	80.8	22.4	61.2	–	None	Traces	0.9	0.7	1.4	1.1	49.0	7.9	4.8	34.5
3	0	113.3	80.9	23.1	59.0	–	None	Traces	0.85	0.7	0.8	1.1	46.7	9.2	4.8	35.8
15	5	121.6	95.0	17.65	66.3	0.15	0.02	Traces	1.1	0.2	3.5	0.7	40.0	15.7	4.2	36.0
16	5	121.6	92.7	19.0	65.6	0.14	0.01	Traces	0.9	0.2	1.6	0.8	38.3	15.0	5.8	35.0
17	10	122	103.1	10.9	69.7	1.43	0.2	0.13	1.8	0.2	7.3	0.8	29.4	21.5	7.0	31.0
18	10	122	102.5	10.4	71.0	1.07	0.1	0.18	1.95	0.1	7.0	0.8	29.4	21.5	5.6	30.7
19	20	123	106.9	8.1	70.3	4.3	0.2	0.51	2.0	0.4	12.1	0.0	26.1	27.5	12.2	21.8
20	20	123	107.5	7.55	70.3	5.7	0.27	0.52	2.4	0.4	12.4	0.6	30.9	28.6	9.6	19.6
21	100	134.8	102.9	14.0	26.4	42.7	0.60	10.0	2.1	3.2	62.5	1.3	5.4	11.1	10.5	4.2
22	100	134.8	103.4	12.95	19.0	51.4	0.52	8.2	2.3	3.7	59.7	0.9	4.3	13.8	11.7	3.5

TABLE 5

Yield of Reaction Products in Tests of the Decomposition of Alcohol–Ethyl Acetate Mixtures and of Ethyl Acetate Alone over an S.V.Lebedev Catalyst

Test No.	Ethyl acetate in alcohol mixture, wt.%	C_4H_6 yield, wt.% based on alcohol: Throughput	C_4H_6 yield, wt.% based on alcohol: Reacted	C_4H_6 yield, wt.%, based on total reacted alcohol and ethyl acetate	Yield: Acetone, wt.%, based on decomposed ethyl acetate	Yield: Alcohol, wt.% based on decomposed ethyl acetate	Per cent: Decomposed alcohol as a percentage of the throughput	Per cent: Decomposed ethyl acetate as a percentage of the throughput
1	0	16.5	33.0	–	–	–	50	–
2	0	18.1	34.1	–	–	–	53	–
3	0	19.4	35.5	–	–	–	54.8	–
15	5	14.6	35.5	31.4	–	–	41.8	97.6
16	5	15.2	35.0	31.2	–	–	43.5	97.7
17	10	8.2	27.5	20.5	1.2	–	29.7	87.7
18	10	7.7	26.8	19.7	1.5	–	28.8	90.8
19	20	5.1	28.5	13.1	3.3	–	17.9	84.0
20	20	4.0	23.0	10.9	3.1	–	17.5	74.4
21	100	–	–	1.7	11.9	31.2	–	66.4
22	100	–	–	1.5	10.9	25.4	–	59.3

to the formation of acetone during the decomposition of the acetic acid, the acetone being reduced by ethyl alcohol to isopropyl alcohol, which splits out water and gives off propylene under the influence of the dehydrating component of the catalyst [17].

In the tests using mixtures of ethyl acetate and alcohol (Table 4), the percentages of carbon dioxide, ethylene, and propylene in the gaseous reaction products increase as the percentage of the ester in the mixture is increased. At the same time the concentrations of divinyl and hydrogen fall off.

The same tests exhibit a rise in the percentages of alcohol, unreacted ethyl acetate, and acetic acid in the liquid reaction products. Some acetone is found in the condensate of the original mixtures that are rich in ethyl acetate. In the tests in which nothing but ethyl acetate was utilized, much of the gas consists of carbon dioxide, the rest consisting of ethylene, propylene, and divinyl. The condensate in the tests using nothing but ethyl acetate contained ethyl alcohol, acetic acid, and acetone (Runs 21-22, Table 4). We also determined the aldehyde and the water-insoluble compounds. Much of the ethyl acetate remained untouched and was carried over into the condensate.

As the percentage of ethyl acetate in the original alcohol mixture is increased (Table 5), the divinyl yield, based on the reacted alcohol, drops off, as do the percentage decomposition of the alcohol and the percentage decomposition of the ethyl acetate.

The conversion of ethyl acetate over an S.V.Lebedev catalyst may be represented as follows: First, the ester is hydrolyzed into acetic acid and alcohol. Then, the resultant acetic acid and alcohol interact as they would under the given conditions. The acetic acid is decomposed to carbon dioxide and acetone; the latter is then reduced by the ethyl alcohol to isopropyl alcohol, which yields propylene when dehydrated. The catalyst converts the ethyl alcohol into ethylene, aldehyde, divinyl, and other products. Part of the alcohol remains unchanged and is found in the condensate. It should be noted that the composition of the gaseous reaction products in the tests using ethyl acetate reminds one of the composition of the gas in the tests using an equimolar mixture of acetic acid and alcohol. This resemblance is further evidence in support of our picture of how the reaction proceeds.

EXPERIMENTAL*

Materials used in the research: rectified ethyl alcohol d_4^{20} 0.8092, containing 93.2% absolute alcohol; acetic acid d_4^{20} 1.051; ethyl acetate, dried and distilled at 76-79°, d_4^{20} 0.8984. The saponification results indicated that the product contained 97.2% of the absolute ester.

The tests with acetic acid had as their aim determining the effect of adding acetic acid to the ethyl alcohol upon the formation of divinyl, and to determine the transformations that the acetic acid undergoes under the reaction conditions. Mixtures of the alcohol and acetic acid, containing 1, 5, 10, and 55.2% by weight (the equimolar mixture of alcohol and acetic acid) were subjected to catalysis over an S.V.Lebedev catalyst; the throughput rate was 1 ml per minute. We also ran tests with acetic acid alone. All the tests were run at the same temperature in a quartz tube with a diameter of 28 mm and 100 mm long, placed in an electric furnace 70 cm long. The catalyst was first subjected to thermal activation, after which 200 ml of the catalyst was placed in the tube.

A thermocouple was placed in a porcelain pocket, the thermocouple junction lying in the center of the catalyst bed. After completion of the run, the catalyst was regenerated by the standard method. A fresh catalyst was substituted after every three or four runs. The reaction products passed through a water-cooled condenser, the condensate being collected in an ice-chilled receiver, and the gas traversing two bottles filled with a normal solution of hydroxylamine hydrochloride to bind the carbonyl compounds and being collected in a gasometer over a saturated solution of sodium chloride.

The unreacted alcohol in the condensate was determined by driving it off by the V.V.Dyakonov method, after the aldehyde had been resinified, the acetone had been taken up (by furfural), and the higher alcohols had been extracted with kerosene. The acetone was determined by the V.V.Chelintsev method [19]; the acetaldehyde was determined by means of hydroxylamine, applying a correction for the acetone; the water-insoluble compounds (liquid hydrocarbons) were washed out with 35 volumes of water; and the acetic acid was titrated with 0.1 N KOH and methyl orange.

In the tests in which a mixture containing 55.2% of acetic acid was used the ethyl acetate was also determined by saponification with a titrated alkali solution; in the alcohol determination a correction was made for the alcohol produced by saponifying the ester.

The gaseous reaction products were analyzed by absorbing them in sulfuric acid of different concentrations by the A.F.Dobryansky method; the carbon dioxide was determined by absorption in a KOH solution; the carbon monoxide by absorption in ammoniacal cuprous chloride; and hydrogen by combustion over palladinized asbestos. The divinyl was determined by the weight of tetrabromobutane required for its bromination.

The results of our tests with acetic acid and with its mixtures with ethyl alcohol are given in Tables 2 and 3. In Test 11, using an equimolar mixture of alcohol and acetic acid, the gas was freed of its CO_2 by passing it

* Performed in 1942 with the collaboration of the technician V.P.Litvinovskaya.

through a 30% solution of NaOH and then fractionated with a column of the Podbilnyak type. We took 9.2 liters of gas, 3.8 liters remaining after the alkali treatment. The fractionation results were as follows:

Waste gas (H_2, CO) 39.3% by volume; C_2 hydrocarbon fraction 16.3%; C_3 26.8%; C_4 11.4%; fractionation residue 6.3%.

The C_3 hydrocarbon fraction was brominated. The bromides were washed free of the bromine, dried, and fractionated in a flask fitted with a dephlegmator.

3.88 g were taken for fractionation: Fraction 1, 138-140°, 0.56 g; Fraction 2, 140-141°, 2.63 g; residue + losses, 0.69 g; d_4^{20} of the 140-141° fraction = 1.9453 (the b.p. of propylene bromide is given in the literature as 141.6° and the d_4^{20} as 1.9333).

Thus, the C_3 hydrocarbon fraction, which constitutes most of the gas, consists of propylene.

In the tests in which nothing but acetic acid was used, the condensate was distilled from a flask fitted with a dephlegmator.

Test 13. 32.54 g taken for fractionation; 57-75° fraction = 20.38 g; residue = 11.78 g; losses = 0.38 g. The 57-75° fraction was dried with anhydrous Na_2SO_4 for two days and then refractionated.

We took 19.25 g for fractionation: 56.5-60° fraction = 14.67 g (nearly all of it distilled at 56.5-57.5°); residue 4.40 g; losses 0.18 g; the d_4^{20} of the 56.5-60° fraction was 0.8017 (the literature gives the b.p. of acetone as 56-57° and its d_4^{15} as 0.7970).

Similar results were secured when we isolated the acetone in Test 14.

The tests with ethyl acetate and its mixtures with ethyl alcohol were run under the same conditions as the tests with alcohol—acetic acid mixtures. We decomposed mixtures containing 5, 10, and 20% of ethyl acetate, as well as the ester by itself. The gas was analyzed as outlined above. The ethyl acetate in the condensate was determined by saponification. The ethyl alcohol was determined by the V.V.Dyakonov method after first having saponified the ethyl acetate with the calculated quantity of 1.5 N KOH. A small amount of furfural was added to the condensate before distilling the alcohol in order to take up the acetone. The total alcohol found was used to compute the alcohol produced during saponification of the ester. The difference was taken as the free ethyl alcohol in the condensate. The aldehyde was determined by the Ponndorf method — oxidizing with wet silver oxide. The acetic acid, the acetone, and the water-insoluble compounds were determined as described above. The test results are given in Tables 4 and 5.

In Test 21, in which nothing but ethyl acetate was used, the carbon dioxide was removed from the gas by passing the latter through an alkali solution and then fractionating it into a Podbilnyak-type column, isolating the hydrocarbon fraction, which was analyzed in an Orsat apparatus.

The waste gas (H_2 + CO + CH_4) was 40.2% by volume; C_2H_4 23.9%; C_3H_6 23.2%; C_4H_8 + C_4H_8 11.1%; residue 1.6%.

Here again, the propylene constitutes a substantial part of the unsaturated compounds in the gas.

SUMMARY

1. An investigation has been made of the conversion of acetic acid and ethyl acetate over the catalyst utilized for the synthesis of divinyl from alcohol. The effect of adding acetic acid and ethyl acetate to ethyl alcohol upon the conversion of the latter to divinyl over the same catalyst has been investigated.

2. It has been shown that these conditions involve the ketonic cleavage of the acetic acid, yielding carbon dioxide and acetone. The yield of the latter was about 70% of the theoretical. When ethyl acetate is decomposed under the same conditions, we get carbon dioxide, acetone, and propylene, on the one hand, and ethyl alcohol, ethylene, acetaldehyde and a small amount of divinyl on the other.

3. The negative effect of adding acetic acid and ethyl acetate to alcohol upon the divinyl yield is due to the conversion that these substances may undergo during the reaction in question.

4. The hypothesis is advanced that carbon dioxide, acetone and propylene may be produced during the S.V. Lebedev catalytic synthesis of divinyl from alcohol in a chain of successive reactions: alcohol → acetaldehyde → ethyl acetate → acetic acid → acetone → isopropyl alcohol → propylene.

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THE FORMATION OF POLYAMIDE RESINS

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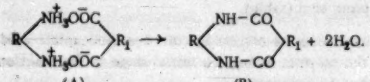
At the present time the reactions involved in the formation of polyamide resins are said to be condensations or polymerizations, depending upon the structure of the initial monomers [1]. If the molecule of the monomer of the polyamide resin is a ring, such as ε-caprolactam, polymerization of the cyclic compounds is the more likely reaction in the process of producing the polymer, according to Knunyants, Rogovin, and others [2]*. The formation of polymers from straight-chain molecules, namely, aliphatic diamines and dicarboxylic acids (more exactly, their salts, is attributed to an ordinary acylation of the amines [1]. There are several arguments, however, against this sort of distinction between the reaction mechanisms resulting in the formation of polyamide polymers. In both cases we get products that differ in no way from one another, except for the number of methylene groups in the structural formations. The technique involved in the production of both polymers is the same. The cyclic structure of the salts of aliphatic diamines and dicarboxylic acids used in the production of polyamide polymers, established by some of the present authors [3], is likewise significant; hence, the first stage of the reaction we are considering must proceed as follows:



(A) (B)

Since structure of the structure of the product (B) closely resembles that of ε-caprolactam, the mechanism of the subsequent reactions ought to be similar in both instances.

The foregoing casts doubt upon the correctness of the distinction made between the mechanism of the reactions involved in the formation of polyamide resins, as governed by the structure of the initial monomers. The elimination of the reasons for making a distinction between the reactions does not, however, mean that either one of them should be preferred in the conversion of rings into polymers.

In considering such transformations we cannot ignore the assertions [4] concerning the identical ability of six-membered rings to undergo reversible polymerization reactions or hydrolysis followed by condensation polymerization. The question then arises: is there a similarity in the transformations of seven- and six-membered rings into polymers, i.e., can polymers be formed from seven-membered rings, especially from ε-caprolactam, by condensation as well as polymerization, as is the case in six-membered rings? It has been said above that at the present time the formation of resins from ε-caprolactam is considered a polymerization process. The inability of N-methylcaprolactam to be polymerized, discovered by Prochazka [5], is cited as proof that no other process is possible in this case. This inability is explained by means of a diagram in which the migration of a hydrogen atom from nitrogen to carbon is specified as the intermediate stage in the polymerization process. Whence it is concluded that caprolactams that are substituted at the nitrogen atom cannot be polymerized [1]. We repeated Prochazka's research on the production of a polymer of N-methylcaprolactam, synthesizing the latter by our own modification of Ruzicka's method [6]. Checking its synthesis by the recently published method outlined by Benson and others [7] did not yield satisfactory results as far as yields were concerned. We found in several samples of N-methylcaprolactam that were heated in sealed ampoules under the conditions employed to polymerize ε-caprolactam, i.e., in an inert medium, with water or dilute acetic acid present, that a temperature in excess of 150° (p = 3 mm) results in the formation of tarred destruction products, a lower temperature yielding the polymer. The reaction product proved to resist heating in an inert medium under pressure better.

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* In a later paper [8], Rogovin, Knunyants, and others do not deny that a condensed polymerization reaction may also be involved in the formation of a polymer; they believe, however, that this latter reaction occurs only in the second stage of the process, the first stage consisting solely of stepwise polymerization.

Effect of Adding ε-Aminocaproic Acid to Caprolactam upon the Polymer's Viscosity

Quantity		Heating time at 240°, hours	Specific viscosity of 0.5% solutions of the polymer in cresol
Aminocaproic acid added to caprolactam, %	Water added to the caprolactam, %		
1	–	0.5	–*
10	–	0.5	0.3
1	–	1	–*
10	–	1	0.39
1	–	3	0.14
10	–	3	0.37
–	10	3	0.31

It should be noted that as the number of substituents at the nitrogen atom is increased, the compounds' resistance to oxidative, temperature, and other agents diminishes.

Thus, the structure of N-methylcaprolactam cannot be resorted to for an explanation of the reactions involved in the formation of polyamide resins from seven-membered rings. The failure of previous attempts to secure a polymer from this compound was due to the sensitivity of the resultant polymers to certain processing conditions, rather than to the absence of a hydrogen molecule attached to the nitrogen atom.

That a condensed polymerization reaction is part of the process of producing a polymer of caprolactam follows from the experiments we have made on the synthesis of polymers from the low-molecular fraction isolated after brief (2 hours) processing of the caprolactam at 230° in ampoules and thorough removal of the caprolactam by washing with ether and dichloroethane. The specific viscosity of the fraction was 0.09; its specific viscosity became 0.6 after heating to 250° (p = 3 mm) for one hour.

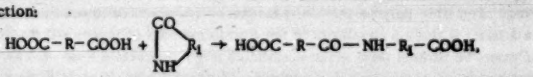
The same conclusion follows from a consideration of the results of the production of polymers of caprolactam in the presence of added ε-aminocaproic acid (table).

The figures in the table indicate increasing the percentage of ε-aminocaproic acid in the reaction mass greatly increases the specific viscosity of the polymer during the initial stage of the reaction; on the basis of stepwise polymerization the contrary should have been expected.

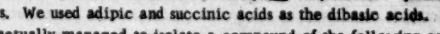
The foregoing justifies the assumption that a condensed polymerization reaction takes place throughout the process of producing the polymer.

Thus, like six-member rings, ε-caprolactam can form a polymer by hydrolysis, followed by a condensed polymerization reaction. Although it is considered to be quite natural that seven-membered rings can be polymerized, and a set of reactions is even adduced for the polymerization of such compounds, no direct proof of such a reaction sequence in the formation of polymers from these ring compounds has ever been given, as far as we know.

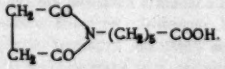
Assuming that such proof would be provided by the synthesis of the intermediate products of the stepwise polymerization reaction:



we tried to isolate them from the products obtained by coupling equimolar quantities of ε-caprolactam and aliphatic dibasic acids. We used adipic and succinic acids as the dibasic acids. When we coupled adipic acid with ε-caprolactam, we actually managed to isolate a compound of the following composition:



Substituting succinic acid for the adipic acid resulted in the formation of ε-succinimidocaproic acid,



We secured the calcium and silver salts of both of these acids. The formation of these products was evidence of the possibility that a polymerization reaction occurred during the conversion of ε-caprolactam into a polymer.

Thus, seven-membered rings, like six-membered rings, may be either polymerized or polycondensed, depending upon the reaction conditions. In the special case in which the reaction is performed in the presence of water, used in sufficient quantity to ensure the hydrolysis of 40-50% of the cyclic monomers, there is no reason to assume that polymerization prevails over condensed polymerization.

*Polymer is water-soluble.

EXPERIMENTAL

Synthesis of N-methylcaprolactam. 2.2 g of metallic sodium was gradually added to a solution of 10 g of caprolactam in 80 g of benzene. Hydrogen was evolved, and a sodium derivative of the caprolactam began to settle out. To precipitate all of it, the mixture was allowed to stand for 24 hours at room temperature. 11 g of dimethyl sulfate was then slowly added to the mixture, which had thickened upon standing. After two days of standing, another 1.1 g of metallic sodium was added to the mixture, followed by 5.5 g of dimethyl sulfate. The precipitated sodium methylsulfate was filtered out and washed with benzene. The benzene solution was processed with a saturated aqueous solution of potash, separated from the latter, and dried with potash. Then the benzene was driven off on a water bath, and the N-methylcaprolactam in vacuo on an oil bath. The latter compound was a colorless, mobile oil with a b.p. of 106-108° (6 mm), which agrees with the figure given in the literature [6].

Production of a polymer of N-methylcaprolactam. 2 g of N-methylcaprolactam was placed in a glass ampoule and diluted with 1 ml of water. Carbon dioxide was used to drive the air out of the ampoule, which was then sealed and heated to 150° on an oil bath for 3 hours. Then the ampoule was cooled, and its contents exposed to the outside air by chipping off the sealed capillary. Then the mixture was heated to 150° in vacuo (p = 5 mm) for 2 hours. This yielded a viscous mass, which solidified into a jelly upon cooling.

0.1277 g subs.: 12.7 ml N_2 (22°, 755.2 mm). 0.1072 g subs.: 10.4 ml N_2 (24.8°, 758.1 mm). Found %: N 11.41, 11.11. $C_7H_{13}ON$. Calculated %: N 11.02.

A sample of N-methylcaprolactam, the processing of which differed only in the use of a higher heating temperature, 200° (p = 5 mm), decomposed, turning into a black liquid.

Coupling adipic acid with ε-caprolactam. A mixture of 1 mole of ε-caprolactam and 1 mole of adipic acid was heated to 240° for 24 hours in a sealed ampoule, from which the air had been driven out with carbon dioxide; then the ampoule's contents were cooled and connected to the outside air, after which the melt was heated in vacuo (p = 5 mm) to 240° for 3 hours. The resultant melt was dissolved in water and treated with an excess of calcium carbonate. The excess $CaCO_3$ was filtered out, and the filtrate was evaporated on a water bath to a syrup containing a high percentage of crystals. The crystals were filtered out, washed with ether, and dried. The percentages of Ca and nitrogen were determined as follows:

0.4820 g subs.: 0.0837 g CaO. 0.4994 g subs.: 0.0880 g CaO. 0.1054 g subs.: 4.5 ml N_2 (22°, 755 mm). 0.1242 g subs.: 5.3 ml N_2 (21.5°, 754.5 mm). Found %: N 4.90, 4.89; Ca 12.41, 12.59. $C_{12}H_{21}O_6NCa$. Calculated %: N 4.41; Ca 12.7.

The solution of calcium salts in water was treated with a 10% solution of silver nitrate. The precipitated silver salt was filtered out, washed with water, and dried.

0.3018 g subs.: 0.1808 g AgCl. 0.3044 g subs.: 0.1828 g AgCl. Found %: Ag 45.0, 45.09. $C_{12}H_{19}O_6NAg_2$. Calculated %: Ag 45.66.

Coupling succinic acid with ε-caprolactam. This coupling and the recovery of the salts were effected as above.

0.5010 g subs: 0.0614 g CaO. 0.4956 g subs.: 0.0611 g CaO. Found %: Ca 8.76, 8.8. $C_{20}H_{32}O_8N_2Ca$. Calculated %: Ca 8.62. 0.3242 g subs.: 0.1418 g AgCl. 0.2416 g subs.: 0.1072 g AgCl. Found %: Ag 33.0, 33.39. $C_{10}H_{16}O_6NAg$. Calculated %: Ag 33.73.

SUMMARY

1. It has been established that in the production of polyamides, seven-membered ring compounds can be converted into polymers in two ways: polymerization and condensed polymerization.

2. Contrary to the statements in the literature [1], reaction conditions have been discovered at which N-methylcaprolactam can form polymers. It has been established that the polymers of N-methylcaprolactam are more sensitive to temperature changes than polymers of seven-membered ring compounds that have no substituents at the nitrogen atom.

3. The products of coupling ε-aminocaproic acid with adipic and succinic acids have been isolated.

4. Adding ε-aminocaproic acid to ε-caprolactam greatly increases the specific viscosity of the polymer at the start of the reaction.*

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* A. Matthes comes to the same conclusion in a paper in Die Makromoleculare Chemie, 5, 197 (1951), which was published after the receipt of the present paper by the editorial board.

** See Consultants Bureau translation, p. 603.

IN MEMORY OF VLADIMIR VASILEVICH CHELINTSEV

K. M. Rodionov and E. K. Nikitin

On April 3, 1952 five years had passed since the death in Saratov of one of the greatest of Soviet scientists, a scientist with immense popularity among teachers and academic and engineering-technical workers of the Central Volga Provinces, distinguished scientist,* corresponding member of the Academy of Sciences of the USSR, Vladimir Vasilevich Chelintsev. In his person were united the eminent chemist and the man of the world, the brilliant teacher and the popularizer, the most active public-spirited worker and the patriot. He embarked on a scientific career at the start of this century and left behind him a very rich scientific legacy in the shape of about one hundred printed scientific papers, monographs, and textbooks, and over 200 published papers on the history of chemistry, and on various technical problems concerning the study of the resources of his country.

V. V. Chelintsev was born on February 22, 1877 in Saratov. His father served in the Zemstvo**, his mother was a teacher in the Saratov High School for Girls. On leaving the Saratov High School Vladimir Vasilevich entered Moscow University where he completed the course in the chemical section of the physico-mathematical faculty. There he attended lectures by the distinguished scientists: N. D. Zelinsky, V. V. Markovnikov, N. N. Lyubavina, V. I. Vernadsky, N. P. Lebedev and others. Vladimir Vasilevich widened the knowledge which he had gained in the university by many visits abroad in which he studied the techniques of such eminent scientists as E. Fischer, Van't Hoff, Pictet, and Grignard.

After completing his course at the university in 1902, V. V. Chelintsev remained as assistant in the department of organic chemistry. In 1908 he became a dozent and in 1910 professor. From 1917 he continuously administered for 30 years the department of organic chemistry at Saratov University.

The life of this distinguished man was so many-sided and rich in content that this short article can hardly go into full details. From the time of completion of the university course up to the last days of his life the intense activity of Vladimir Vasilevich was spread over four departments: scientific, pedagogic, scientific popularizing and public service.

Vladimir Vasilevich started his scientific career as an independent researcher in 1902. His first investigation in the field of organometallic compounds served to bring him to the notice of a series of eminent chemists of the day. The papers of the young Russian investigator, V. V. Chelintsev, published in Russian and foreign journals were concerned with both the theory of the formation of "ethereal organomagnesium compounds" (then still a completely virgin field) and the discovery of new "organomagnesium halides". These were hailed in the world chemical literature as an original stage in the development of our knowledge of organometallic compounds. In later work in the same sphere, V. V. Chelintsev showed, firstly, that the ether in the Grignard reaction is not merely a solvent but also a catalyst; secondly, that organometallic compounds can be prepared not only by the catalytic action of ether but also by that of tertiary amines with replacement of the medium by benzene; and thirdly, that in the latter case, using small proportions of tertiary amines, "unusual compounds" are obtained.

Chelintsev's researches gained him a prize from the Moscow Chemical Society whose president at that time was Professor V. V. Markovnikov. This was five years after V. V. had completed the university course.

* An honorary title in the USSR. (Publisher's note)

** A rural self-government organization in prerevolutionary Russia. (Publisher's note)

In subsequent investigations V. V. Chelintsev showed that the action of ethers, sulfides and tertiary amines on certain organomagnesium compounds (presenting the appearance of a snow-white solid mass) suspended in benzene leads to conversion of the organomagnesium compounds into complexes soluble in excess of the added substances. Vladimir Vasilevich thereby demonstrated that certain organomagnesium compounds are converted into oxonium, thionium and ammonium complexes. He then carried out, in the celebrated thermochemical laboratory of V. F. Luginin, careful investigations of the heat of formation of the above-mentioned compounds and of the heat of decomposition of the final complexes with water.

These determinations supplied the first data for the relative thermal effects of the formation of oxonium, thionium and ammonium complexes and for the influence of organic radicals on these magnitudes. In these researches he moved on to a new field of immense importance, namely the higher valences of organic compounds containing oxygen, nitrogen and sulfur. Pursuing his investigations in this direction, V. V. Chelintsev extended them to all classes of organic compounds – alcohols, ethers, phenols, ketones, esters, etc. His many investigations, which attracted general attention for their fundamental character and novel content, enabled him to show that these higher valences varied in dependence on the different functional groups in organic compounds. In the opinion of Academician A. E. Favorsky, these were classical investigations in the field of the oxonium compounds.

On the basis of the thermochemical investigations, V. V. Chelintsev was able to correct the earlier formulas of complex oxonium compounds, for example that of dimethylpyrrole advanced by Collis, Bayer, Villiger and others. These studies yielded a complete table of the thermochemical data relating to higher valences in all the basic groups of organic compounds. On the basis of this table we can now fairly readily predict which of these substances will displace other compounds from complexes during their interaction; the table also supplies information on the effect on these transformations of functional groups, organic radicals, and other substituents.

After studying organomagnesium compounds under laboratory conditions, V. V. Chelintsev went over to the study of such compounds in nature – in the field of chlorophyll. Here he threw light upon a series of problems; firstly, the position of magnesium in the pyrrole rings and the significance of this grouping; secondly, the configuration of the complex chlorophyll molecule with reference to the appearance in nature of a system containing four pyrrole rings in spite of the fact that two rings would have sufficed for the absorption of carbon dioxide; thirdly, the chemistry of assimilation. For these objectives he synthesized a series of magnesium-substituted pyrroles, worked out a series of new methods, and obtained such new compounds as pyrrole glycols and pyrroledicarboxylic acids. These investigations were fruitful for pyrrole chemistry in general.

In attempting to solve the second problem of the configuration of the complex chlorophyll molecule, V. V. Chelintsev investigated the condensation of pyrrole with acetone and showed that the pyrrole ring has an innate tendency to form those tetranuclear complex systems on which chlorophyll is based, and that the condensation of two-ring systems is inevitably followed by transformation into tetranuclear systems. In this manner he solved the problem of the formation in nature (in chlorophyll) of complex groupings of pyrrole rings.

Concerning the third problem – the mechanism of absorption of carbon dioxide during assimilation and its subsequent reduction – V. V. Chelintsev was not satisfied with Willstatter's scheme involving participation of the magnesium-substituted chlorophyll rings. V. V. obtained substituted acids by reacting carbon dioxide with such magnesium-substituted simplest pyrrole derivatives, and no reduction of the carbon dioxide was observed. He himself proposed a mechanism for the reaction of carbon dioxide with water under the influence of chlorophyll followed by formation of sugar.

From 1930 V. V. Chelintsev devoted his energy to the study of furan compounds and their condensations. He worked out a special method for isolating furfural from the products of distillation during the manufacture of furfural from vegetable materials. He examined the colored compounds prepared by condensing furfural with various organic compounds. On the basis of these coloring matters he and his students developed methods of determination of small amounts of acetone, furfural, formaldehyde and acetaldehyde. The work of V. V. Chelintsev on the preparation of alcohols and ketones of the furan series has considerably widened our knowledge of the chemistry of furan compounds.

V. V. Chelintsev realized a series of new syntheses also in other branches of organic chemistry: The synthesis of α-keto acids with the aid of copper cyanide; the synthesis of chalconogenic ketones; the synthesis of isomeric ketones and of unsaturated ketones with the help of magnesium-substituted aminates; the synthesis

of new crystalline complexes of ketones and esters with acids, phenols, and quinones. These investigations signposted new synthetic routes and stimulated a whole series of new researches and new ideas which left their mark in the Russian and foreign scientific literature.

V. V. Chelintsev was a member of several chemical societies. In 1933 he was chosen as corresponding member of the Academy of Sciences of the USSR, and in 1935 he was raised to the rank of "distinguished scientist".

V. V. Chelintsev was an outstanding teacher. He lectured on inorganic and organic chemistry, on chemical methodics and on the history of chemistry for over 40 years in the university and the teachers' training college. His lectures were always carefully thought out and brilliant in form. They were simple, clear, correlated with the development of the problems discussed, and were always accompanied by a series of striking experiments. They were also attended by students in other courses as well as by teachers who wished to learn how to clarify chemical problems and to perform experiments. Vladimir Vasilevich loved chemistry and had an instinct for the experimental side.

V. V. Chelintsev was a great patriot. He understood the necessity of popularizing knowledge, of making propaganda for science and of popularizing it among the vast masses. He wrote a series of books in popular language under the titles of "Organic chemistry and biographies of its outstanding figures", "Fundamental chemical concepts, laws and theories in popular presentation", "Rivalry between the laboratory and nature", "The centenary of the birth of Louis Pasteur", etc. He organized the Saratov Chemical Society and the Saratov Teachers' Naturalist Society and served them faithfully and incessantly. With his feverish energy and inexhaustible initiative, Chelintsev interested himself passionately in the problems of the chemical industry, in the development and exploitation of the natural resources of the country and in particular of his native region of Privolzh. He prepared reports for special industrial conferences in diverse national committees and in the Academy of Sciences with reference to the development of the natural wealth of the country.

Over a period of many years V. V. Chelintsev acted as consultant and fellow-worker of the Saratov "kraisovnarkhoz". He published numerous papers on the mineral and vegetable wealth of the region and undertook in the university laboratory many investigations of specimens of raw materials from different parts of the Volga Province and other regions. He was interested in petroleum, peat, shale, gases, salts, clays, pyrites and sands. He was interested in such industries as drying oils, glues, tanning agents, and hydrogenation of fats. He entered all these fields as a penetrating researcher, as a great patriot, as a pioneer in problems of technology, and as an industrial organizer.

The Government of the USSR showed high appreciation of the services of Vladimir Vasilevich Chelintsev. He was twice awarded the "Red Banner of Labor" and received a medal "for valiant service in the Great Patriotic War".

Vladimir Vasilevich devoted all his energies to the organization and prosperity of the beloved university of his native town and to the development of the natural resources of his region. He always expressed himself an enthusiastic believer in the possibilities of development of the chemical industry of the Volga Province and showed keen interest in the development of culture in Saratov, the town in which N. G. Chernyshevsky (of whom Chelintsev liked so often to talk) was born and died.

In V. V. Chelintsev Soviet chemistry has lost an outstanding scientist, a richly endowed investigator with a wide range of scientific interests who devoted all his knowledge, skill and energy to the service of the country and science. The death of Chelintsev was felt in particular by his pupils, whose link with him was never broken up to the last days, and also by Saratov University where he worked from its foundation.

The luminous figure of Chelintsev — teacher and friend — will always remain in the recollection of his pupils and comrades, while his achievements will serve for many long years as an example to fresh generations of investigators and will occupy one of the most honored places in the history of organic chemistry. His pupils will exert every effort to compensate for this heavy loss and together with the whole army of Soviet chemists they will pursue the extensive development of chemical science for the glory of our socialist state.

THE MOST IMPORTANT PUBLICATIONS OF V. V. CHELINTSEV*

I. Papers in Scientific Journals

[1] The action of isopropyl iodide on magnesium. J. Russ. Chem. Soc. 36, 549 (1904).

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THE SOLUBILITY OF CALCIUM MOLYBDATE

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Precipitation of calcium molybdate is utilized in analytical chemistry for the quantitative determination of molybdenum [1] and calcium [2] and for separation of the latter from magnesium [3]. A number of authors have proposed to separate molybdenum in the form of calcium molybdate from industrial solutions during the processing of molybdenum ores [4,5]. However, the literature contains very little information about the solubility of calcium molybdate. According to Smith and Bradbury [1] this compound is partially soluble in water and insoluble in alcohol. Dittler [6] measured the solubility of calcium molybdate in water at temperatures of 30° and 170°. In the latter case a saturated solution was obtained at high pressure. The solubility on a molybdenum basis was (per 100 ml water) 0.0055 g at 30° and 0 0328 gat 170°. Bashilov and Kindyakov [5] determined the solubility of calcium molybdate in water at a temperature of 18° and obtained a value of 0.017 g per 100 ml (likewise calculated as molybdenum).

We have studied the solubility of calcium molybdate in water by gravimetric and colorimetric methods at various temperatures between 0° and 100°.

I. Preparation and Analysis of Normal Calcium Molybdate

Calcium molybdate was prepared by reacting (at room temperature) solutions of sodium molybdate and calcium chloride containing equimolecular amounts of these substances. The precipitate was washed for a prolonged period with water by the decantation method until chlorine ions had been completely removed. Washing was continued as long as the turbidity, developed after addition of silver nitrate to a sample, did not begin to dissolve completely in dilute nitric acid. The precipitate was drained on a Buchner funnel and dried in the air at room temperature.

The water content of the preparation was determined by calcination at 500° to constant weight, and the mean value found was 4.87% (the hemihydrate, $CaMoO_4 \cdot 0.5H_2O$, corresponds to 4.30%). Consequently our air-dried preparation approximates to the hemihydrate. The slightly high water content may be explained by the fine dispersion of the precipitate and its large surface, in consequence of which it heavily adsorbs water. The calcined preparation was analyzed for its content of calcium and molybdenum.

For the determination of calcium, about 0.2 g (exactly weighed) of the molybdate was dissolved in 20 ml of 35% hydrochloric acid, and calcium oxalate was precipitated from the solution by the usual method. Since it is more convenient in the final stage to weigh calcium sulfate rather than calcium oxide, the calcium oxide resulting from the calcination of the oxalate was moistened with water and then worked up with a few drops of conc. sulfuric acid. The mixture was evaporated to dryness and then calcined at a temperature of 500-600°.

For the determination of molybdenum the weighed sample (of the order of 0.1 g) was dissolved in sulfuric acid and precipitation was effected with α-benzoin oxime [7]. The precipitate was converted into molybdic anhydride by calcination at 500° and weighed.

The analytical results are presented in Table 1.

TABLE 1
Analysis of Calcium Molybdate

	CaO (%)	MoO_3 (%)
Found content...	28.03	71.94
	28.00	71.96
Mean	28.01	71.95
Calculated for $CaMoO_4$ . .	28.04	71.96

The contents of calcium oxide and molybdic anhydride in the preparation are close to the theoretical.

2 Study of the Solubility of Calcium Molybdate in Water by the Gravimetric and Colorimetric Methods

We investigated the solubility of calcium molybdate at temperatures of 0, 22, 50, 65, 75, 80, 90 and 100°.

Experiments in the temperature range of 22-90° were performed in a glass test-tube with a spiral stirrer and an oil seal for protection of the solution against evaporation and entry of dust from the air. 75 ml distilled water was introduced into the test-tube followed

by a weighed amount of about 0.4 g calcium molybdate. The test-tube was placed in a thermostat whose temperature was kept constant by means of an electric heater with a contact thermometer. The temperature was observed to fluctuate in the range of ± 0.5°. Observations at 0° were made with the thermostat filled with snow and water. The mixing of the liquid with the calcium molybdate was usually effected continuously over a period of several days.

The determination of solubility at 100° was performed with the help of a 1-liter flask fitted with a 12-bulb reflux condenser. The flask contained 750 ml distilled water and 4 g calcium molybdate. Boiling was continued for 48 hours in order to establish equilibrium. In these experiments the temperature variations were likewise within the limits of ± 0.5°.

Samples of the solution were withdrawn with glass pipets whose ground-glass tips contained a filter plate of porous glass. A small piece of cotton wool was also placed beneath the filter. The pipet was wrapped in cotton wool to guard the solution against changes of temperature. Establishment of equilibrium was checked with the help of control samples which were analyzed colorimetrically for their molybdenum content.

The molybdenum was determined colorimetrically by Chernikov's method [8], involving the formation of a colored complex of the composition (according to Babko [9]) $Mo(CNS)_5$. A Duboscq colorimeter was used for comparing the color intensities.

Gravimetric determination of the solubility was carried out when the concentration of molybdenum in the liquid phase had become constant. A sample of the solution was transferred to a weighing bottle. The weight of the solution was found and then evaporation was performed in a drying cupboard. The solid residue was brought to a constant weight at 200°. A determination was also made of the content of anhydrous salt in 100 g of solution. The minute amount of adsorbed water remaining in the preparation after drying under the stated conditions does not exceed 0.1% and may be ignored. The solubility of calcium molybdate in 100 ml of solution was determined colorimetrically. The experimental data are presented in Tables 2 and 3 and plotted in the diagram.

TABLE 2

Solubility of Calcium Molybdate (Method of evaporation of solution)

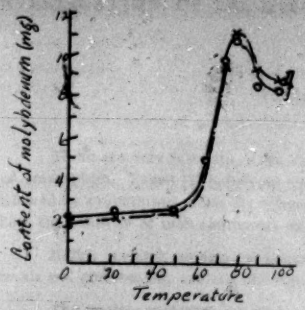
Temp.	Expt. No.	Wt. of solution, g	Wt. of dry residue	Amount of dry substance in 100 g of solution	Mean, g	Molybdenum content of 100 g of solution	Solubility of the salt in moles/100 g solution
0°	1	25.93	0.0012	0.0046	0.0046	0.0022	$2.3 \cdot 10^{-4}$
	2	23.45	0.0011	0.0046			
22	1	19.82	0.0010	0.0052	0.0052	0.0025	$2.6 \cdot 10^{-4}$
	2	21.67	0.0012	0.0052			
50	1	19.63	0.0011	0.0057	0.0056	0.0027	$2.8 \cdot 10^{-4}$
	2	17.98	0.0010	0.0056			
65	1	52.27	0.0052	0.0099	0.0102	0.0049	$5.1 \cdot 10^{-4}$
	2	56.13	0.0060	0.0106			
75	1	51.53	0.0106	0.0205	0.0204	0.0098	$1.2 \cdot 10^{-3}$
	2	31.49	0.0063	0.0203			
80	1	39.56	0.0089	0.0226	0.0227	0.0109	$1.13 \cdot 10^{-3}$
	2	29.39	0.0067	0.0229			
90	1	52.73	0.0093	0.0177	0.0178	0.0087	$8.9 \cdot 10^{-4}$
	2	56.86	0.0102	0.0179			
100	1	40.77	0.0072	0.0176	0.0177	0.0085	$8.8 \cdot 10^{-4}$
	2	53.77	0.0096	0.0178			

TABLE 3

Content of Molybdenum in 100 ml of Saturated Solution of Calcium Molybdate (Colorimetric Method)

Temperature	0°	22°	50°	75°	80°	90°	100°
Content of molybdenum in 100 ml solution (g)	0.0019	0.0022	0.0025	0.0095	0.0112	0.0095	0.0090
Solubility of the salt (in moles per liter)	$2.0 \cdot 10^{-4}$	$2.3 \cdot 10^{-4}$	$2.6 \cdot 10^{-4}$	$9.9 \cdot 10^{-4}$	$1.16 \cdot 10^{-3}$	$9.9 \cdot 10^{-4}$	$9.4 \cdot 10^{-4}$

The analyses of the solid phase from the experiments on determination of the solubility of calcium molybdate showed that its composition did not differ from that of the starting preparation. It can therefore be concluded that no hydrolytic processes took place during the action of water on the calcium molybdate.



Solubility of calcium molybdate at various temperatures. I) Molybdenum content (by gravimetric method) in mg/100 g solution. II) Molybdenum content (by colorimetric method) in mg/100 ml solution.

The mean accuracy of the colorimetric determination of molybdenum for the given concentrations is 5-10%. We can therefore consider the agreement between the colorimetric method and the evaporation method to be quite satisfactory. Attention may be drawn to the higher values in the literature for the solubility of calcium molybdate in water at around room temperature.

The data of Tables 2 and 3 (see also the diagram) indicate that the solubility of calcium molybdate increases continuously from 0 to 80° and then declines. In this behavior calcium molybdate is reminiscent of gypsum whose solubility curve passes through a maximum at 38°. We are of the opinion, however, that in the case of calcium molybdate the inflection point on the solubility curve corresponds to a change in the hydrated state of the salt.

SUMMARY

1. The solubility in water of normal calcium molybdate was investigated over the temperature range of 0-100°.

2. Colorimetric determination of the molybdenum content and determination by the method of evaporation of saturated solutions of calcium molybdate gave results in close agreement.

3. The solubility curve of calcium molybdate is characterized by an inflection point (maximum) at a temperature of 80°.

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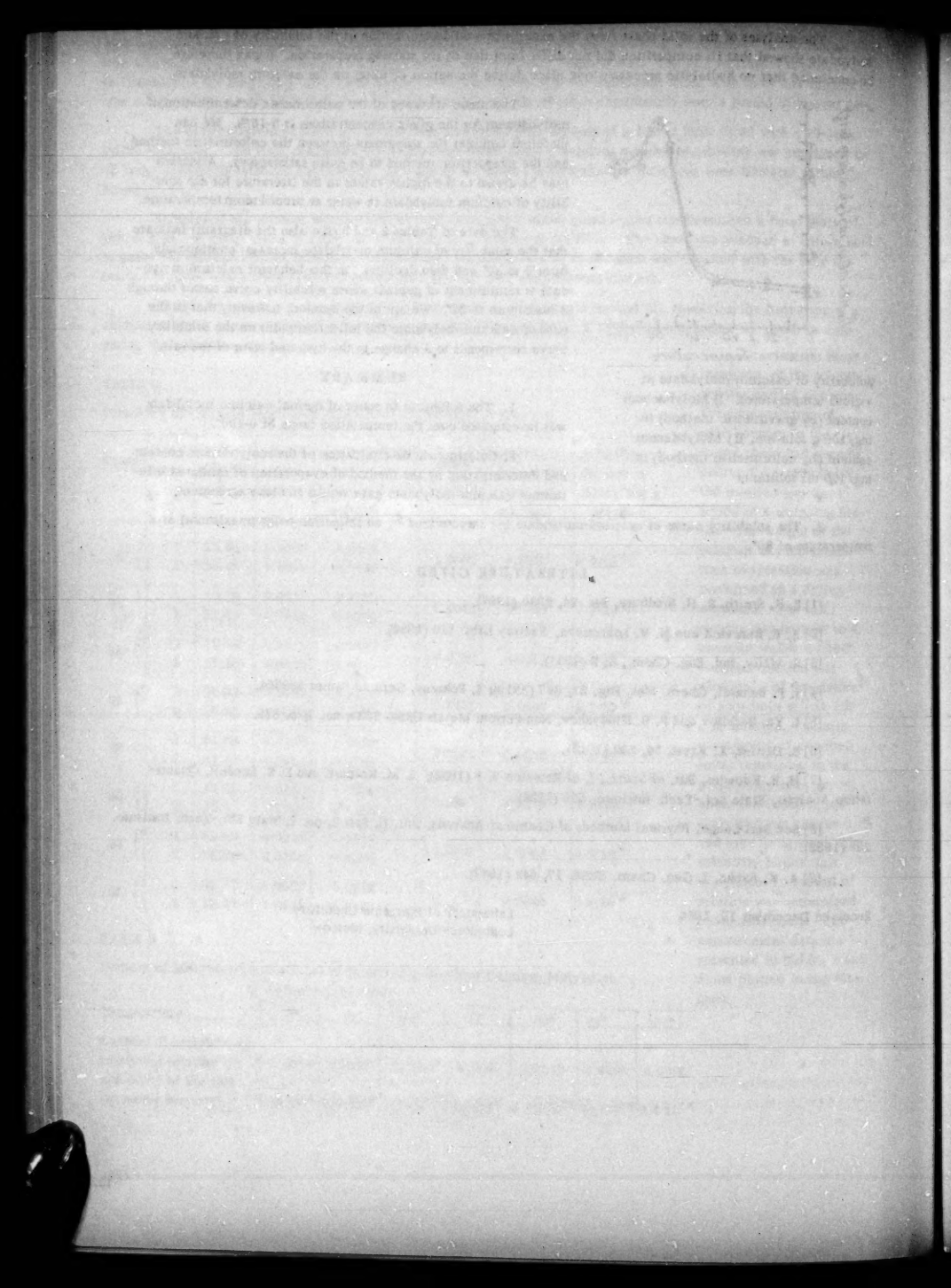

INVESTIGATION OF THE MIXED SULFATES OF THE ALKALI ELEMENTS AND AMMONIUM

Vikt. I. Spitsyn and M. A. Meerov

There are very few data in the literature on the preparation of mixed sulfates of the alkali elements and ammonium. Troost [1] points out that reaction of solutions of the normal sulfates of lithium and ammonium followed by evaporation yields the lithium-ammonium sulfate $Li_2SO_4 \cdot (NH_4)_2SO_4$. No information is available about the behavior of such compounds when heated.

In this research we have investigated the conditions of preparation of mixed sulfates of all of the alkali metals and ammonium, and also the thermal stability of these compounds.

The starting materials for the preparation of the compounds were the pyrosulfates of the alkali elements which we described previously [2]. Weighed amounts of the pyrosulfates in procelain crucibles were dissolved in small amounts of water; the solutions were treated with concentrated ammonia and left to evaporate in desiccators over phosphorus pentoxide. After a few days crystallization of the salts commenced. The crucibles with their contents were removed from the desiccators and crystallization was completed in the air over a period of 9-10 days.

TABLE 1

Analysis of the Mixed Sulfates of the Alkali Elements and Ammonium

Compound	SO_3 content, %	
	found	calculated
$LiNH_4SO_4$	66.22	66.14
$NaNH_4SO_4$	58.32	58.40
KNH_4SO_4	52.59	52.26
$RbNH_4SO_4$	40.23	40.11
$CsNH_4SO_4$	32.38	32.41

Determinations of the SO_3 content (and in some cases of the NH_3) were carried out by the usual methods on the air-dry crystals. All of the isolated salts had a composition represented by the formula $MeNH_4SO_4$, where Me is an alkali element. See Table 1 for the analytical results.

In the mixed rubidium-ammonium sulfate the ammonia content was also determined and was found to be 8.25%, as compared with 8.51% for $RbNH_4SO_4$.

The structure of the compounds remains unclarified since the data agree equally well with the formulas $MeNH_4SO_4$ and $Me_2SO_4 \cdot (NH_4)_2SO_4$.

If we assume the first formula to be the more probable, we may express the formation reaction by the following equations:

$$Me_2S_2O_7 + H_2O = 2MeHSO_4; \quad MeHSO_4 + NH_3 = MeNH_4SO_4.$$

In Figure 1 is a photograph of the lamellar crystals of cesium-ammonium sulfate which readily aggregate into large concretions. (See plate p. 1521).

The thermal stability of the mixed sulfates was investigated by heating weighed amounts in porcelain crucibles in a drying cupboard or in an electric furnace until constant in weight. Analyses of the final products showed that these were always the pyrosulfates.

The decomposition of the mixed sulfates evidently proceeds according to the equation:

$$2MeNH_4SO_4 = Me_2S_2O_7 + 2NH_3 + H_2O.$$

We did not observe the formation of hydrosulfates as intermediate products.

In Table 2 are detailed the start of conversion of the mixed sulfates into pyrosulfates, the yield of the latter, and the experimental and theoretical contents of SO_3 in the products obtained. These data indicate that the thermal stability of the mixed sulfates of the alkali elements and ammonium increases in passing from lithium to cesium. The potassium-ammonium and rubidium-ammonium sulfates have similar decomposition temperatures. The most

TABLE 2

Heating of the Mixed Sulfates of the Alkali Elements and Ammonium

Compound	Initial temp. of conversion to pyrosulfate	Yield of $Me_2S_2O_7$ from $MeNH_4SO_4$ (in % of theory)	% SO_3 content in the final product	
			found	calcd. for $Me_2S_2O_7$
$LiNH_4SO_4$	100-130°	99.14	84.09	84.27
$NaNH_4SO_4$	150-170	98.59	72.03	72.09
KNH_4SO_4	170-190	100.39	62.59	62.96
$RbNH_4SO_4$	170-200	99.31	46.04	46.14
$CsNH_4SO_4$	270-300	99.78	36.29	36.23

stable of the compounds prepared is cesium-ammonium sulfate.

In a previous investigation we established the thermal conditions for transformation of the hydrosulfates of the alkali metals into pyrosulfates [3]. It may be noted that for the sulfates of lithium-ammonium, sodium-ammonium and potassium-ammonium the temperature of initial decomposition only exceeds by 10-20° the temperature of transition of the corresponding hydrosulfates into pyrosulfates, while in the case of rubidium-ammonium sulfate and rubidium hydrosulfate these temperatures coincide. By contrast, cesium-ammonium sulfate decomposes at a temperature 120° higher than the decomposition temperature of the corresponding hydrosulfate.

In all cases the decomposition temperatures of the mixed sulfates lie considerably below the temperatures of initiation of transformation of the pyrosulfates into the normal sulfates. Consequently the addition of ammonia to pyrosulfates fails to facilitate the process of transformation of the latter into normal sulfates by heating.

Just as in the case of hydrosulfates [3], the stability of the investigated mixed sulfates is observed to increase with increasing atomic number of the alkali elements. This is clearly bound up with the reduced polarizing action of cations with increase in their radii, which leads to weakening of the contrapolarization in HSO_4^{-2} or $NH_4SO_4^{-2}$ ions.

It is interesting to note that the addition of ammonia to the HSO_4^{-1} ion has no marked effect upon the thermal stability of the compound. We may conclude that the bonding of hydrogen with the SO_4^{-2} ion has the same effect upon the properties of the mixed sulfate as it has upon the properties of the hydrosulfate.

SUMMARY

1. Mixed sulfates of all of the alkali elements and ammonium of the general composition $MeNH_4SO_4$ were prepared by crystallization of ammoniacal solutions of pyrosulfates.

2. The prepared compounds decompose on heating and are transformed into the pyrosulfates.

3. The temperatures of this transformation to pyrosulfates increase with increasing ionic radius of the alkali elements and are close to the temperatures of conversion of the corresponding hydrosulfates to pyrosulfates.

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SOME TERNARY COMPLEXES OF COPPER AND SILVER

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In recent times numerous investigations have been made of the formation and stability of so-called "ternary complexes", i.e. complex compounds containing various addenda and one and the same central ion.

A. K. Babko [1] adduced weighty evidence for the existence of such compounds in the system copper-pyridine-salicylate and studied their stability. Meites [2] detected the complexes $[Cu_4(OH)_4C_2O_4]$ and $[Cu(OH)_2cit_2]^{6-}$ and used a polarographic method to measure their stability constants. The complexes of $[Hg_2Cl_2(C_2O_4)_2]^{2-}$ have also been formed and their stability measured[3]. Salts of copper and silver evidently possess a strong tendency to form mixed complexes. Salts of the type of $nCuX \cdot mRX \cdot R_2S_2O_3$, for example, were prepared by Rosenheim and Steinhauser [4], Canneri and Luchini [5], and others. (In the foregoing formula X is halogen or CNS^-, and R is a cation of ammonium or an alkali metal). Similar salts containing a silver cation were also prepared [4].

For the purpose of ascertaining whether ternary complexes can exist in solution, we have made a study of the solubility of CuI and CuCNS in $Na_2S_2O_3$ solution. It was conjectured that if evidence could be obtained that the reaction took place in accordance with the following scheme:

$$MX_{solid} + I^-_{aq} = MXI^-_{aq} , \qquad (I)$$

the problem would be clarified and an explanation obtained of the phenomena accompanying the solution of silver halides in potassium thiocyanate solutions [6]. Randall and Halford [6] drew attention to the futility of interpreting the results obtained with the aid of any simple assumptions.

Thiosulfate and halide complexes of silver and copper have been studied by numerous investigators. The abundance of the published material in this field makes it impossible to compile even a brief summary of the literature. We shall limit ourselves to remarking that in spite of the large number of publications devoted to thiosulfate complexes of copper, the stability constants of these complexes have never been measured. On the other hand the stability constants of the halide complexes of copper and silver, also of the thiosulfate complexes of silver, have been determined by many authors [7,8,9,10].

EXPERIMENTAL

As mentioned above, we used the solubility method to test the above hypothesis of the existence of mixed complexes in aqueous solutions.

The choice of cupric iodide and thiocyanate was dictated by their constancy of composition and their ease of preparation. Both of the compounds are formed from components in strictly stoichiometrical ratios. They were synthesized in accordance with the procedures of quantitative analysis from chemically pure reagents ($CuSO_4 \cdot 5H_2O$; KI; KCNS; and $Na_2S_2O_3 \cdot 5H_2O$.)

The prepared salts were thoroughly washed with water and introduced in the moist form into solutions of sodium thiosulfate. Solution of the solid phase was effected by continuous agitation over a period of several days until the establishment of equilibrium in the system at a temperature of $25 \pm 0.1°$. After reaching equilibrium the solutions were analyzed for their content of $S_2O_3^{2-}$ and Cu^+. Both of the ions were determined iodimetrically. The former ion was titrated immediately by the direct or reverse method (by introducing an excess of iodine and back-titrating). For determination of Cu^+ the solution was first freed from $S_2O_3^{2-}$ by heating with conc. HNO_3 and the latter was removed by evaporation with H_2SO_4. In the case of solutions with a high concentration of $S_2O_3^{2-}$ an analysis was made of the solid phase which always contained Cu and CuCNS. Results are presented in Tables 1 and 2.

EVALUATION OF RESULTS

On analyzing the compounds which they had isolated, Ryabchikov and Silnichenko [11] came to the conclusion that salts of the following types can be obtained in aqueous solutions: $Me[Cu(S_2O_3)]$, $Me_4[Cu_3(S_2O_3)_5]$ and $Me_3[Cu(S_2O_3)_2]$.

TABLE 1

Solubility of CuI in Solutions of Sodium Thiosulfate

No.	Molarity·10³			$\frac{[Cu^+]}{[S_2O_3^{2-}]}$
	$Na_2S_2O_3$			
	Total	free	CuI	
1	1.927	0.372	1.555	4.18
2	3.624	0.844	2.780	3.29
3	4.210	0.764	3.446	4.51
4	7.029	1.759	5.270	3.00
5	7.940	1.856	6.084	3.28
6	8.708	2.054	6.654	3.24
7	18.05	4.20	13.85	3.30
8	32.54	7.51	25.03	3.33
9	44.20	10.65	33.55	3.15
10	53.76	10.94	42.82	3.91
		Mean value		3.52

TABLE 2

Solubility of CuCNS in Solutions of Sodium Thiosulfate

No.	Molarity·10³			$\frac{[Cu^+]}{[S_2O_3^{2-}]}\cdot 10$
	$Na_2S_2O_3$			
	Total	free	CuCNS	
1	1.720	1.383	0.3368	2.43
2	2.109	1.690	0.4194	2.48
3	3.542	2.772	0.7705	2.78
4	4.900	3.935	0.9652	2.45
5	6.370	5.065	1.305	2.58
6	7.750	6.002	1.748	2.91
7	11.94	9.118	2.822	3.09
8	18.41	14.11	4.304	3.05
9	24.32	18.19	6.127	3.37
10	33.72	25.08	8.645	3.45
11	42.46	31.45	11.01	3.50
12	52.16	38.62	13.54	3.51
13	83.23	59.25	23.98	4.05
		Mean value		3.05

However, in a solution of copper iodide in sodium thiosulfate, ions of $CuS_2O_3^-$, $[Cu_2(S_2O_3)_3]^{4-}$ and $[Cu(S_2O_3)_2]^{3-}$ are apparently not formed. The impossibility of existence of the latter two ions follows from the fact that the formation of such complexes would necessitate the combination of $\frac{3}{2}$ or 2 molecules of $Na_2S_2O_3$ with each ion of copper. In solution, however, the ratio $[Na_2S_2O_3]:[CuI]$ never reaches these values but always remains below 1.35.

If the dissolution of CuI in $Na_2S_2O_3$ solution had proceeded according to the scheme:

$$CuI_{solid} + S_2O_3^{2-} = CuS_2O_3^- + I^-, \qquad (II)$$

then the solubility of CuI in $Na_2S_2O_3$ would have changed proportionally to the square root of the concentration of free thiosulfate. The data of Table 1 show, however, a linear dependence. These inconsistencies can be readily eliminated if we assume that the process of dissolution of CuI in $Na_2S_2O_3$ proceeds according to the equation:

$$CuI_{solid} + S_2O_3^{2-} = [CuIS_2O_3]^{2-}, \qquad (III)$$

$K = 3.5 \pm 0.5$; $\Delta z = -742$ cal.

The calculated values of the equilibrium constant for reaction (III) are listed in Table 1. Here the value of the constant is 3.5 ± 0.5 on condition that the activity coefficients of $CuIS_2O_3^-$ and $S_2O_3^{2-}$ ions are equal. On the basis of this value of the equilibrium constant we have calculated the change in thermodynamic potential (Δz).

The formation of the complex ion $[CuIS_2O_3]^{2-}$ appears to us more probable than the simultaneous existence in the solution of $CuS_2O_3^-$ and I^- ions since the latter manifest a marked tendency to enter into firm combination with Cu^+ and its independent existence is improbable.

The change in solubility detailed above might be explicable through the formation of ions of $Cu(S_2O_3)_2^{3-}$ and of CuI_2^- in equi-ionic ratios, but we are hardly entitled to assume the absence of reaction between these ions.

The equilibrium constant of reaction (III) is related to the solubility product of CuI and to the stability constant of the $[CuIS_2O_3]^{2-}$ complex by the expression:

$$K = \frac{Pr}{K_N} \qquad (1)$$

where K is the equilibrium constant of reaction (III), Pr is the solubility product of CuI, and K_N is the stability constant of the $[CuIS_2O_3]^{3-}$ complex. If we take the value of $1.1 \cdot 10^{-12}$ [13] for Pr_{CuI}, we find for K_N:

$$\frac{[Cu^+][I^-][S_2O_3^{2-}]}{[CuIS_2O_3^{3-}]} = 3.1 \cdot 10^{-13}.$$

On the basis of the above expressions we have assumed a similar solution mechanism for CuCNS:

$$CuCNS_{solid} + S_2O_3^{2-} = [Cu(CNS)S_2O_3]^{3-}. \qquad (IV)$$

$K = 0.30 \pm 0.05$; $\Delta z = 713$ cal.

The equilibrium constant for reaction (IV) is given in Table 2. It is equal to 0.30 ± 0.05. In this case, however, a small but appreciable rise in the constants is observed with increasing $Na_2S_2O_3$ concentration. We might explain this phenomenon either by inconstancy of the ratio of the activity coefficients or by the formation of complexes with a larger number of coordinated $S_2O_3^{2-}$ ions. If such complexes were indeed formed, then their concentration — judging by the magnitude of the change in the equilibrium constant — must be low.

The solubility product of CuCNS is equal to $4 \cdot 10^{-14}$ [13], and therefore the stability constant of $[Cu(CNS)S_2O_3]^{3-}$ is

$$\frac{[Cu^+][CNS^-][S_2O_3^{2-}]}{[Cu(CNS)(S_2O_3)^{3-}]} = 1.3 \cdot 10^{-13}.$$

The similarity between the stability constants of both of the ternary complexes is striking. By assuming that the formation of the ternary complexes according to scheme (I) occurs fairly frequently, we find an explanation of the hitherto puzzling data of Randall and Halford [6]. Dissolution of AgCNS in KCNS solution can only lead to formation of ions of the type of $[Ag(CNS)_n]^{1-n}$. Analysis of the data of Randall and Halford shows that the reaction in this case proceeds according to the equation:

$$AgCNS_{solid} + 3CNS^- = [Ag(CNS)_4]^{3-}. \qquad (V)$$

$K = 1.2 \pm 0.5 \cdot 10^{-1}$; $\Delta z = 1255$ cal.

The equilibrium constant of this reaction is found to be $1.2 \pm 0.5 \cdot 10^{-1}$ (Table 3).

TABLE 3

Solubility of Silver Thiocyanate in Potassium Thiocyanate Solutions

Expt. No.	Molarity			$\frac{[AgCNS]}{[KCNS]^3} \cdot 10^3$
	$AgCNS \cdot 10^3$	KCNS		
		total	free	free
1	2.02	0.312	0.306	0.029	7.03
2	12.1	0.564	0.528	0.147	8.23
3	45.8	0.870	0.732	0.393	11.6
4	98.5	1.124	0.829	0.570	17.1

Mean value $12 \pm 5 \cdot 10^{-2}$

The solubility product of AgCNS is equal to $1.16 \cdot 10^{-12}$. Using this value we find for $[Ag(CNS)_4]^{3-}$ a stability constant of $1.0 \pm 0.5 \cdot 10^{-11}$.

This value is in good agreement with the stability constant of $Ag(CNS)_3^{2-}$, found by Ferrell and co-workers by the e.m.f. method [10]. For the $[Ag(CNS)_3]^{2-}$ complex Ferrell and co-workers found a value of $K_N = 1.7 \cdot 10^{-11}$, and for $[Ag(CNS)_2]^-$ a value of $K_N = 2.0 \cdot 10^{-11}$.

The solubility of AgI in KCNS changes linearly with the change in KCNS concentration (Table 4), as can be seen from the results of Randall and Halford. These results, however, are not distinguished by a high degree of accuracy.

In order to account for the linearity of the dependence of the solubility on the KCNS concentration, we may put forward two reaction schemes:

$$AgI_{solid} + 2CNS^- = (Ag(CNS)_2]^- + I^-; \qquad (VI)$$

$$AgI_{solid} + CNS^- = [AgICNS]^-. \qquad (VII)$$

$K = 1.2 \pm 0.7 \cdot 10^{-4}$; $\Delta z = 5345$ cal.

Scheme (VI) proposed by the authors is hardly probable on two grounds: Firstly, it is difficult to accept the possibility of displacement of iodine ions into the outer shell by the less firmly bound thiocyanate ions; secondly, the

calculation of the stability constant of $[Ag(CNS)_2]^-$ according to scheme (VI) gives a value of the order of 10^{-9}, which is inconsistent with the data presented above. Calculation of the equilibrium constant of reaction (VII) leads to a value of $1.2 \pm 0.7 \cdot 10^{-6}$. The stability constant of $[AgICNS]^-$ calculated on this basis is equal to $7.1 \cdot 10^{-23}$ ($Pr_{AgI} = 8.5 \cdot 10^{-17}$). This result is in good accord with literature data for complexes of the $[AgX_n]^{1-n}$ type with iodide and thiocyanate.

TABLE 4

Solubility of Silver Iodide in KCNS Solutions

Expt. No.	Molarity $AgI \cdot 10^6$	KCNS total	KCNS free	$\frac{[AgI]}{[KCNS]} \cdot 10^6$
1	0.20	0.202	0.202	0.99
2	0.14	0.315	0.315	0.44
3	0.67	0.425	0.425	1.57
4	0.51	0.500	0.500	1.02
5	0.40	0.608	0.608	0.66
6	0.97	0.710	0.710	1.36
7	1.46	0.765	0.765	1.91
8	1.63	1.009	1.008	1.63
		Mean value		$1.2 \pm 0.7 \cdot 10^{-6}$

S. I. Burmistrov directed our attention to the fact that in the case of dissolution of AgBr in KCNS the solid phase must be silver thiocyanate and not bromide (on the basis of the ratio of the solubility products). Our experiments showed indeed that in this case AgCNS is precipitated, so that all the data of Randall and Halford relating thereto are erroneous.

In conclusion we may point out that the fairly old data of Valenta [12] on the solubility of silver halides in sodium thiosulfate solutions confirm our theory that the reactions do not proceed according to the equation:

$$AgX_{solid} + S_2O_3^{2-} = AgS_2O_3^- + X^- \qquad (VIII)$$

but according to the equation:

$$AgX_{solid} + S_2O_3^{2-} = [AgXS_2O_3]^{3-}. \qquad (IX)$$

A third possibility of formation of complexes of the type of $[Ag(S_2O_3)_2]^{3-}$ when dissolving silver chloride in sodium thiosulfate solutions is excluded by the fact that the ratio of the concentration of sodium thiosulfate to the concentration of dissolved silver chloride never reaches a value of 2.

Scheme VIII is rather improbable because the solubility changes linearly with increasing concentration of sodium thiosulfate and not in proportion to the square root of this concentration. Furthermore, the calculation of the stability constant of the $AgS_2O_3^-$ ion, starting from the solubility of AgCl, AgBr and AgI, leads to three different results, namely:

$$0.7 \cdot 10^{-9},\ 2.0 \cdot 10^{-13} \text{ and } 1.1 \cdot 10^{-13}.$$

Consequently all the data support the scheme IX. The equilibrium constants and the changes in free energy have the following values:

$AgCl_{solid} + S_2O_3^{2-} = AgClS_2O_3^{2-}$. $K = 2.2 \pm 0.4$; $\Delta z = -466.6$ cal.

$AgBr_{solid} + S_2O_3^{2-} = [AgBrS_2O_3]^{3-}$. $K = 0.8 \pm 0.2$; $\Delta z = 132.1$ cal.

$AgI_{solid} + S_2O_3^{2-} = [AgIS_2O_3]^{3-}$. $K = 3.2 \pm 0.2 \cdot 10^{-2}$; $\Delta z = 2038$ cal.

Below are given the stability constants calculated from the preceding data:

$$\frac{[Ag^+][Cl^-][S_2O_3^{2-}]}{[AgClS_2O_3^{2-}]} = 0.7 \cdot 10^{-13}; \quad \frac{[Ag^+][Br^-][S_2O_3^{2-}]}{[AgBrS_2O_3^{3-}]} = 4.1 \cdot 10^{-13}; \quad \frac{[Ag^+][I^-][S_2O_3^{2-}]}{[AgIS_2O_3^{3-}]} = 2.7 \cdot 10^{-13}.$$

All of the considerations put forward above support the assumption that ternary complexes are formed fairly frequently. The necessity for their investigation has been clearly revealed. We may add that in the light of the ideas here developed, great caution should be applied when making calculations of the equilibria between a precipitate and a solution containing complexing ions.

SUMMARY

1. It has been established by an analysis of our experimental data and of the data of other workers that when halides of copper (I) and silver dissolve in thiosulfate solutions, mixed complexes of the type of $[MeXS_2O_3]^{3-}$ are formed.

2. The solubility of CuI and CuCNS in thiosulfate solutions was measured at various temperatures and calculations were made of the stability constants of the resultant $[CuIS_2O_3]^{3-}$ and $[Cu(CNS)S_2O_3]^{3-}$ ions; the respective values were $3.1 \cdot 10^{-13}$ and $1.3 \cdot 10^{-13}$.

3. On the basis of literature data for the solubility of silver halides in thiocyanate and thiosulfate solutions the stability constants of the following ions were calculated: $[Ag(CNS)_4]^{3-}$, $[AgICNS]^-$, $[AgClS_2O_3]^{3-}$, $[AgBrS_2O_3]^{3-}$, $[AgIS_2O_3]^{3-}$.

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PHYSICO-CHEMICAL INVESTIGATION OF THE PHOSPHORUS TRICHLORIDE–BROMINE SYSTEM. II.

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An investigation of the PCl_3–bromine system by the method of thermal analysis [1] revealed the formation of two compounds: PCl_3Br_4 (orange-red prisms melting at 37.5°) and PCl_3Br_{18} (long cherry-red needles melting at 24.5°). Both of these compounds were obtained in the pure state. They proved to be fairly strong electrolytes; the specific electric conductivity of these complexes in the fused state at 45-65° is of the order of 10^{-4} $ohm^{-1}cm^{-1}$.

Consideration of the mechanism of formation and chemical nature of these chlorobromides of phosphorus led to the suggestion that PCl_3Br_4 and PCl_3Br_{18} are polybromides – products of addition of bromine to initially formed PCl_3Br_2. In this connection it was conjectured that in the system PCl_3–bromine may be formed not only PCl_3Br_4 and PCl_3Br_{18} but also other chlorobromides with different amounts of bromine (>4 and <18), whose existence for some reason or other was not manifested on the fusion diagram.

The aim of the present investigation was to continue the foregoing work in order to obtain a deeper insight into the characteristics of these complex compounds, and also in order to obtain further evidence for the proposed mechanism of formation and for the nature of these higher phosphorus halides.

For the purpose of determining the composition of the complex in the liquid phase the viscosity of the system PCl_3–Br_2 was studied. In addition, electrochemical investigations were made of these complexes in organic solvents.

Viscosity of the System PCl_3–Br_2

The viscosity was determined with the help of the apparatus and method described in the paper by Ya.A. Fialkov and L.D.Muzik [2] with the sole difference that all the tubes through which air passed were fitted with calcium chloride tubes since the investigated system is extremely hygroscopic.

The solutions for the viscosity measurements were prepared as follows: an exact amount of bromine was weighed into a small conical flask which could be closed with a ground-glass stopper; a 50 cc separating funnel, on which was placed a rubber stopper which formed a good fit on the flask, was weighed separately. Into this separating funnel was weighed a quantity of PCl_3 sufficient to give a solution of a definite concentration. The separating funnel was then attached to the flask with the help of the rubber stopper. The flask was stood in cold water (the reaction between PCl_3 and bromine is accompanied by considerable evolution of heat) and PCl_3 was run dropwise into the bromine. The funnel was then lifted off and the flask closed with the glass stopper. The mixture was shaken for several minutes and then transferred to the viscosimeter.

Viscosity measurements were performed at temperatures of 25 and 40°. The thermostat was a 5-liter bath filled with water. Temperature variations did not exceed $\pm 0.1°$. The liquid existed in the supercooled state at concentrations exceeding 25 mole % at 25°.

The specific gravities, required for the viscosity calculations, were determined in a pycnometer with an expansion in the upper part of the capillary. Viscosities were determined on the identical solutions whose viscosities were to be measured.

The viscosity and specific gravity data are given in Table 1 and Figure 1. On this diagram the fusibility curve of the same system is shown for comparison.

The absolute viscosity was calculated from the expression:

$$\eta = \eta_0 \frac{dt}{d_0 t_0},$$

TABLE 1

Viscosity of the System PCl_3—Br_2

PCl_3 (mole %)	η (in centipoises)		d - specific gravity	
	25°	40°	25°	40°
Br	1.305	1.131	3.118	3.065
1.31	1.439	–	3.125	–
6.24	2.345	–	3.138	–
10.45	3.458	3.269	3.142	3.123
12.21	5.882	4.147	3.145	3.112
14.31	8.491	5.608	3.128	3.096
17.07	12.722	7.508	3.066	3.032
20.03	13.061	7.719	3.032	2.997
23.49	13.015	7.580	2.961	2.924
24.71	12.624	–	2.921	–
27.22	11.058	6.329	2.846	2.809
28.92	11.014	6.371	2.850	2.815
33.33	11.734	6.793	2.874	2.839

where η_0 is the absolute viscosity of water at the temperature of measurement [3], d_0 and t_0 are the specific gravity and period of efflux of water [3], $\underline{d}$ and $\underline{t}$ are the specific gravity and period of efflux of the investigated system.

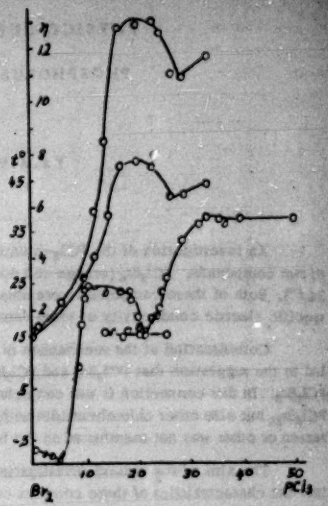

Fig. 1. Diagram of the and viscosity of the system PCl_3—Br_2

The table and diagram show that the viscosity isotherm of the system PCl_3—Br_2 is characterized by a flat maximum whose position does not change with rising temperature.

The maximum viscosity is at a concentration of 20 mole % PCl_3, which corresponds to the formation of the complex compound PCl_3Br_2.

With further rise of concentration (above 20 mole %) the viscosity isotherm at first descends smoothly and then more abruptly, reaching a minimum at 27-28 mole % PCl_3, after which it rises until the content of PCl_3 is 33 mole % and layer separation occurs [1].

The viscosity of fused PCl_3Br_4, i.e., the viscosity of the system PCl_3—Br_2 at a PCl_3 content of 33 mole %, was measured in the following manner: excess of PCl_3 was added to bromine until stratification occurred. After crystallization of the lower layer (PCl_3Br_4), the upper layer (saturated solution of PCl_3Br_4 in PCl_3 which had a constant viscosity) was poured off, and the reaction vessel (a test tube drawn out at several places) was sealed and placed in the upturned position for a period of days until the liquid was completely filled with crystals. The part of the test tube containing the crystals was detached, the crystals were fused and their viscosity measured at 25° (in the supercooled state).

Electric Conductivity of Solutions of Phosphorus Chlorobromides in Organic Solvents

It had been observed when measuring the electric conductivity of PCl_3Br_4, PCl_3Br_8 and PCl_3Br_{18} in the fused state [1] that their conductivity increases with increasing Br content; with rising temperature the conductivity at first rises and then falls.

Since these conductive complexes are thermally unstable, it may be suggested that their thermal dissociation:

$$PCl_3(Br_2)_{n+1} \rightleftarrows PCl_3(Br_2)_{n-1} + Br_2 \cdots \rightleftarrows PCl_3 + nBr_2,$$

leading ultimately to nonconductive substances (PCl_3 and Br_2), decreases with increasing bromine content.

For the purpose of further examination of this phenomenon, we decided to study the electric conductivity of PCl_3Br_4, PCl_3Br_8 and PCl_3Br_{18} in an organic solvent (nitrobenzene)

TABLE 2

PCl_3Br_4 – Nitrobenzene System

PCl_3Br_4 (mole %)	Specific electric conductivity
1.36	$1.07 \cdot 10^{-4}$
3.75	$2.48 \cdot 10^{-4}$
5.33	$2.90 \cdot 10^{-4}$
6.41	$5.47 \cdot 10^{-4}$
7.63	$6.49 \cdot 10^{-4}$
13.49	$1.05 \cdot 10^{-3}$
14.53	$1.15 \cdot 10^{-3}$
24.60	$1.49 \cdot 10^{-3}$
36.53	$1.81 \cdot 10^{-3}$
41.21	$2.11 \cdot 10^{-3}$
48.77	$2.43 \cdot 10^{-3}$
49.01	$2.54 \cdot 10^{-3}$
55.60	$2.86 \cdot 10^{-3}$
61.60	Part of sample did not dissolve

TABLE 3

PCl_3Br_8 – Nitrobenzene System

PCl_3Br_8 (mole %)	Specific electric conductivity
2.76	$1.41 \cdot 10^{-3}$
6.05	$4.80 \cdot 10^{-3}$
16.02	$1.35 \cdot 10^{-2}$
23.43	$1.89 \cdot 10^{-2}$
33.68	$2.49 \cdot 10^{-2}$
40.56	$2.67 \cdot 10^{-2}$
50.41	$3.23 \cdot 10^{-2}$
55.06	$3.41 \cdot 10^{-2}$
83.11	$4.03 \cdot 10^{-2}$
100.0	$4.21 \cdot 10^{-2}$

TABLE 4

PCl_3Br_{12} – Nitrobenzene System

PCl_3Br_{12} (mole %)	Specific electric conductivity
6.46	$1.02 \cdot 10^{-2}$
10.76	$1.67 \cdot 10^{-2}$
16.25	$2.41 \cdot 10^{-2}$
30.79	$3.87 \cdot 10^{-2}$
39.77	$4.56 \cdot 10^{-2}$
50.12	$5.08 \cdot 10^{-2}$
56.24	$4.32 \cdot 10^{-2}$

Nitrobenzene was selected because it is a good solvent for the complexes in question and forms conductive solutions; also it is adequately stable in presence of the phosphorus chlorobromides (it is not brominated by them under the experimental conditions). The PCl_3Br_4 and PCl_3Br_{12} were prepared as described in the previous paper [1]; the PCl_3Br_8 was prepared by mixing PCl_3 and bromine in stoichiometrical proportions.

The specific electric conductivity of all of the solutions was measured at $20 \pm 0.1°$. Results appear in Tables 2-4 and in Figure 2.

The electric conductivity of solutions of PCl_3Br_4 and PCl_3Br_8 rises rapidly with increasing concentration (this is particularly conspicuous in PCl_3Br_{12} solutions), and then slows down until values of the order of 10^{-4} ohm^{-1}cm^{-1} are obtained. The electric conductivity of PCl_3Br_{12} solutions also increases with the concentration but relatively slows, and in the concentration region of more than 53 mole % it even falls off slightly. A comparison of the data of Tables 2-4 and of the isotherms shows that in general the electric conductivity of the investigated solutions increases in the order $PCl_3Br_4 < PCl_3Br_8 < PCl_3Br_{12}$, in analogy with the behavior of these substances in the fused state.

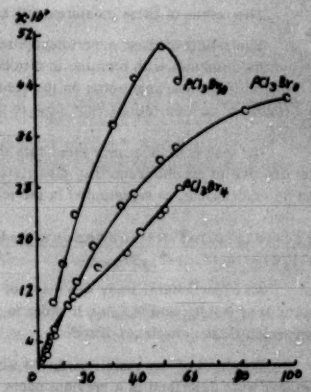

Figure 2. Specific electric conductivity of nitrobenzene solutions of PCl_3Br_4, PCl_3Br_8, and PCl_3Br_{12}.

Measurements were also made of the electric conductivity (at some concentrations) of PCl_3Br_4 in acetonitrile in order to establish the order of magnitude of the conductivity. Such solutions are considerably better conductors than the nitrobenzene solutions especially in the region of low concentrations.

PCl_3Br_4 (mole %)	Specific electric conductivity
2.48	$9.28 \cdot 10^{-4}$
5.52	$2.08 \cdot 10^{-3}$
10.23	$3.38 \cdot 10^{-3}$

Benzene solutions of PCl_3Br_4, PCl_3Br_8 and PCl_3Br_{12} do not conduct electricity, nor do the solutions in CCl_4 and CS_2.

On dissolving these complexes in toluene and acetone a violent bromination reaction takes place, accompanied by evolution of gases.

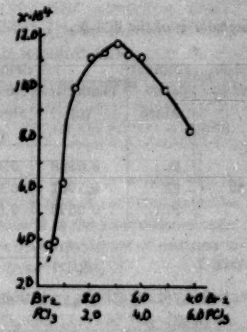

Fig. 3. Specific electric conductivity of the system PCl_3–Br_2 in nitrobenzene

Measurement of the Electric Conductivity of the System PCl_3–Br_2 in Nitrobenzene

These measurements were performed for the purpose of supplementing the foregoing investigations of nitrobenzene solutions of PCl_3Br_4

and other complexes and with the special aim of establishing which of these chlorobromides predominates in nitrobenzene solutions of the system PCl_3-Br_2 containing various ratios of the components.

In order to ensure that these measurements should give results approximating to those of physico-chemical analysis we used the method of Ostromyslensky [4], Job [5], i.e., we prepared equimolecular solutions of PCl_3 and bromine in nitrobenzene and for each experiment we took that number of milliliters of these solutions which resulted only in a change in the ratio of PCl_3 to Br_2 while the total number of moles remained constant. Since the solutions of PCl_3 and bromine in nitrobenzene (taken separately) do not conduct electricity, we could utilize direct experimental data for graphical representation of the results of measurements (i.e., without determining deviations from additivity).

The results of these measurements are presented in Table 5 and Figure 3.

TABLE 5

Electric Conductivity of the System PCl_3-Br_2 in Nitrobenzene

Ratio of volumes (ml) of solutions of Br_2 and PCl_3	Specific electric conductivity at 20°
9.5:0.5	$3.66\cdot10^{-4}$
9.3:0.7	$3.77\cdot10^{-4}$
9.0:1.0	$6.13\cdot10^{-4}$
8.5:1.5	$9.85\cdot10^{-4}$
8.0:2.0	$1.12\cdot10^{-3}$
7.5:2.5	$1.13\cdot10^{-3}$
7.0:3.0	$1.17\cdot10^{-3}$
6.5:3.5	$1.13\cdot10^{-3}$
6.0:4.0	$1.11\cdot10^{-3}$
5.0:5.0	$1.11\cdot10^{-3}$
4.0:6.0	$8.11\cdot10^{-4}$

The results of these experiments strengthen the supposition that phosphorus trichloride combines with bromine in nitrobenzene solutions to form phosphorus chlorobromides. The maximum on the electroconductivity isotherm corresponds to a region of concentrations very close to the composition of the complex PCl_3Br_4.

We may conclude from these data that when the phosphorus chlorobromides dissolve in nitrobenzene they dissociate with cleavage of part of the bromine and an equilibrium, as represented in the schema on p. 1336 is established.

Electrolysis of Nitrobenzene Solutions of PCl_3Br_4 and PCl_3Br_{18}

An experimental study was made of the ionic transfer in nitrobenzene solutions of PCl_3Br_4 and PCl_3Br_{18} in order to investigate the nature of the ions into which these complexes dissociate.

The form of the vessels used, the working procedure and the analytical methods were described in a previous paper [6].

The duration of electrolysis was 1) 4 hours and 2) $6\frac{1}{2}$ hours; the current strength was 1) 4.5 A and 2) 15 A. During electrolysis the color of the anodic liquid gradually darkened, but the cathodic liquid became considerably lighter in color.

The results of these experiments are shown in Tables 6 and 7.

TABLE 6

Electrolysis of the $PCl_3Br_4-C_6H_5NO_2$ System

PCl_3Br_4 (Wt.%)	Element determined	Catholyte			Anolyte		
		Theoretical (g)	Found after electrolysis (g)	Difference (g)	Theoretical (g)	Found after electrolysis (g)	Difference (g)
9.66	Br....	0.5956	0.4828	−0.1128	0.6911	0.8018	+0.1108
	Cl....	0.1981	0.2708	+0.0727	0.2298	0.1543	−0.0755
	P.....	0.0578	0.0756	+0.0178	0.0631	0.0452	−0.0179

TABLE 7

Electrolysis of the $PCl_3Br_{18}-$Nitrobenzene System

PCl_3Br_{18} (Wt.%)	Element determined	Catholyte			Anolyte		
		Theoretical (g)	Found after electrolysis (g)	Difference (g)	Theoretical (g)	Found after electrolysis (g)	Difference (g)
15.28	Br....	1.0424	0.8136	−0.2288	1.3099	1.5304	+0.2205
	Cl....	0.0962	0.1539	+0.0577	0.1201	0.0599	−0.0602
	P.....	0.0314	0.0545	+0.0231	0.0393	0.0164	−0.0228

On calculating the ratios in which phosphorus and chlorine migrate to the anolyte, we find that each atom of phosphorus corresponds to the following numbers of gram-atoms of chlorine: 3.6 (in experiments with PCl_3Br_4) and 2.3 (in experiments with PCl_3Br_{18}). The corresponding figures for bromine are: 2.5 (with PCl_3Br_4) and 4.8 (with PCl_3Br_{18}).

The smaller amount of bromine transferred to the anolyte is evidently due to partial decomposition of the complexes in nitrobenzene

solution, this process being accompanied by cleavage of part of the bromine content, in consequence of which the investigated solutions actually contain complexes whose bromine content is lower than would correspond to their composition in the solid state. Furthermore, if we start from the general formula which we suggested for these complexes, $[PCl_3Br][Br(Br_2)_n]$, then part of the bromine must migrate to the cathode in the form of a complex cation, and this would also slightly reduce the quantity of bromine in the anodic portion of the solution.

EVALUATION OF THE RESULTS

Comparing the results of investigation of the system PCl_3-Br_2 with the experimental data presented in the first communication [1], we must first direct attention to the disagreement between the results of thermal analysis and of determination of the viscosity of the system.

The fusion diagram of the system PCl_3-Br_2 revealed the formation of two complexes $-PCl_3Br_4$ and PCl_3Br_{18}. These investigations failed to reveal the existence of PCl_3Br_8 which has been mentioned in the literature [7]. In the concentration region (20 mole % PCl_3) corresponding to this complex we found on the fusion diagram a eutectic with m.p. 15.1-15.5°. On the other hand the change in viscosity points to the existence of the complex PCl_3Br_8 in the liquid phase. The flat maximum is evidence of the instability of this complex.

A similar type of phenomenon has been noted in the literature, mainly in the papers of N.S.Kurnakov and his co-workers. For example, Kurnakov, Krotkov and Oksman [8] investigated the system $SbBr_3-(C_6H_5)3CH$ and found on the viscosity isotherms a maximum which did not change with the temperature, and on the fusion diagram only one eutectic, the viscosity maximum corresponding to the concentration region close to the eutectic composition.

Analogous observations were made by A.Vinogradova and N.Efremov [9], and by A.Tikhomirova and N. Efremov [10], in examining the systems phenol – methyl (or dimethyl) aniline and phenol – ethyl (or diethyl) aniline.

The absence of a maximum on the fusion diagram can be accounted for by the unfavorable conditions of crystallization of PCl_3Br_8 in the viscous medium.

Our experiments actually showed that the viscosity of the system PCl_3-Br_2 at a content of 20 mole % PCl_3 (at 25°) is nearly ten times higher than the viscosity of bromine. The viscosity isotherms of the system PCl_3-Br_2 are further characterized by the following features: a) The temperature coefficient of the viscosity is low at first but increases with the PCl_3 concentration and reaches a high value in the concentration region coinciding with the viscosity maximum, which provides further confirmation of the existence of the complex PCl_3Br_8 in the liquid phase. b) A minimum is observed on the viscosity isotherms in the region of 27-28 mole % PCl_3, following which the viscosity increases continuously up to the point of stratification of the system at a content of 33 mole % PCl_3, which corresponds to the complex PCl_3Br_4, and then the viscosity of the lower layer (fused PCl_3Br_4) becomes constant. Consequently the viscosity isotherms reflect the existence of this complex in addition to that of PCl_3Br_8.

The fact that the viscosity isotherm does not reflect the existence of PCl_3Br_{18} can be ascribed to partial dissociation of the complex in the liquid phase or to the general phenomenon that in the case of some complexes existing in the liquid phase, only those that are more stable under the experimental conditions are usually reflected on the viscosity diagram.

The measurement of the viscosity of PCl_3-Br_2 has thus supplemented our earlier results by showing that the existence of still another complex is possible in the liquid phase. The formation of the phosphorus chlorobromides of the general formula $PCl_3 \cdot (Br_2)_n$, discussed in this paper, may be considered to proceed in the following manner: during the action of bromine on PCl_3, oxidation of the latter first takes place to the accompaniment of addition to it of one mole of bromine and the formation of the simplest chlorobromide of this type $-PCl_3Br_2$. *

When PCl_3Br_2 reacts with excess of bromine the former behaves like a halide of pentavalent phosphorus. As we know, PCl_5 and PBr_5 are capable of adding on bromine, when the complexes $PCl_5 \cdot 5Br_2$ [11] and $PBr_5 \cdot (Br_2)_n$ are formed, n being equal to 1.2 and 6 [12].

It may be assumed that the pentavalent phosphorus in this reaction, just as during interaction with iodine halides [6], is polarized according to the scheme $PX_5 \rightarrow [PX_4]X$; the anion X in the outer shell coordinates the molecules of halogens, iodine and chloride, iodine bromide, etc., which simultaneously strengthens the structure of the complex with the halogen-substituted phosphonium cation.

* As stated in the literature [13], this compound is extremely unstable and only exists at low temperatures. It decomposes when heated. Its instability is associated with stratification of the system PCl_5–bromine when the PCl_3 content exceeds 33 mole %.

On the basis of the preceding hypothesis, the following scheme may be advanced for the reaction of PCl_5 with bromine, it being assumed that the excess of bromine adds on to the bromine anion of the outer shell:

$$PCl_5 \xrightarrow{+Br_2} PCl_5Br_2 \longrightarrow [PCl_5Br]Br \xrightarrow{+Br_2} [PCl_5Br][Br(Br_2)_n].$$

The magnitude of n may vary from 1 to 8.

Consequently the simplest of these polybromides is $[PCl_5Br][Br(Br_2)]$ or PCl_5Br_6, while the most complex is $[PCl_5Br][Br(Br_2)_8]$ or PCl_5Br_{18}.

The results of experiments on the migration of ions in nitrobenzene solutions of the system PCl_5–Br_2 generally confirm the above structure of these phosphorus chlorobromides. The relative thermal instability of these complexes is consistent with the assumption that various intermediate forms between PCl_5Br_6 and PCl_5Br_{18} can exist in the fused state or in solution. It is to be hoped that these diverse complexes (with various magnitudes of n) will also be isolated in the crystalline form.

Although these phosphorus chlorobromides are relatively unstable, they do not undergo complete decomposition into the original PCl_5 and Br_2 when fused. The fused complexes have a high electric conductivity which first rises with the temperature and then (starting from 45-50°) falls off. On the other hand, PCl_5 and bromine in the free state do not conduct electricity at all.

The fact that the electric conductivity of the phosphorus chlorobromides increases in the order of PCl_5Br_6–PCl_5Br_8–PCl_5Br_{10}, i.e. with increasing bromine content, may be explained by the shifting to the left of the equilibrium of dissociation of these complexes:

$$PCl_5(Br_2)_n \rightleftarrows PCl_5(Br_2)_{n-1} + Br_2 \ldots \rightleftarrows PCl_5 + nBr_2.$$

SUMMARY

1. The viscosity of the system PCl_5–Br_2 was measured at 25 and 40° when a maximum was found at 20 mole % PCl_5, corresponding to a complex of the composition PCl_5Br_8. Two other complexes — PCl_5Br_6 and PCl_5Br_{10} — are indicated on the fusion diagram of this system.

2. The electric conductivity of these complexes in nitrobenzene solution increases with the concentration, attaining values of the order of 10^{-2} $ohm^{-1}cm^{-1}$, and also increasing in the order $PCl_5Br_6 < PCl_5Br_8 < PCl_5Br_{10}$.

3. Measurement of the electric conductivity of the system PCl_5–Br_2 in nitrobenzene by the method of isomolar concentrations (method of Ostromyslensky and Job) revealed the formation of products of addition of bromine to PCl_5, with PCl_5Br_6 as the most probable composition.

4. By means of the method of ionic migration it was shown that the structure of these phosphorus chlorobromides can be expressed by the following general formula: $[PCl_5Br][Br(Br_2)_n]$. On the basis of thermal analysis of the system PCl_5–Br_2 and of investigations of the synthesis of chlorobromides, we may assume that n ranges between 1 and 8, which corresponds to the series of complexes starting from PCl_5Br_6 and finishing at PCl_5Br_{18}.

In their chemical nature these complexes may be regarded as polyhalides of tetracidophosphonium cations.

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OXIDATION POTENTIALS OF HYPOCHLORITE SOLUTIONS

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The oxidizing ability and the character of the oxidizing action of hypochlorites depend in large measure upon the activity of the hydrogen ions in their solutions.

The dependence of the oxidizing properties on the pH is undoubtedly associated with the nature of hypochlorite solutions and certain features of the equilibria which are established in these solutions.

In 1900 were published the classic studies of Professor A. A. Yakovkin on the equilibrium of chlorine hydrolysis [1]:

$$Cl_2 + H_2O \rightleftharpoons H^+ + Cl^- + HClO, \qquad (1)$$

The hydrolysis constants which he obtained enable exact relations to be found between the chlorinating and the true oxidizing action of hypochlorites. A good deal of work has been devoted to the determination of the dissociation constant of hypochlorous acid, and values usually within the range of 10^{-8}–10^{-7}, have been reported. The equilibria of the two processes – hydrolysis of chlorine and dissociation of hypochlorous acid – govern the state of a solution of hypochlorous acid at different pH values.

Calculations show that alkaline solutions (pH $>$ 10) contain substantially only ClO^- ions. Solutions whose pH is in the range 8.5–6.0 contain hypochlorous acid and its salt in approximately equal amounts. Solutions whose pH is below 5 are substantially free from salt.

Strongly acid solutions (pH $<$ 3) contain, in addition to hypochlorous acid, appreciable amounts of chlorine ions. The ratio of the two components in such solutions at various pH values is governed by the hydrolysis constant of chlorine.

Hypochlorite solutions are not equilibrium systems by virtue of the fact that slow processes of decomposition accompanied by formation of chlorates or oxygen proceed arbitrarily in them.

The stability of these solutions is determined by the pH. Thus it has been found that the mechanism of conversion of hypochlorite into chlorate varies according to whether the reaction proceeds in alkaline, neutral or acidic media. The velocity of the process likewise varies. The latter was found [2] to be a minimum in a strongly acidic medium (pH $\cong$ 1); with increasing pH it rises and attains a maximum in a nearly neutral medium (pH $\cong$ 6.7); the conversion velocity begins to fall again in an alkaline medium.

We see that the activity of H^+ ions is one of the fundamental factors governing not only the oxidizing properties of hypochlorite solutions but also their composition and stability. An accurate characterization of this influence would clearly permit a deeper insight into the properties and nature of hypochlorite solutions. More precise knowledge of the effect of pH on the oxidizing properties may be obtained by an investigation of the oxidation potentials of these solutions.

Very few papers have been published on the dependence of oxidation potentials on pH in hypochlorite solutions, and these publications are lacking in full details of either the oxidation potentials themselves or of the equilibria governing them. We were therefore prompted to carry out an investigation of the dependence of the oxidation potentials of hypochlorite solutions on the pH.

EXPERIMENTAL

In alkaline solutions of hypochlorite the oxidation potential may be governed by electrode reaction:

$$ClO^- + 2H^+ + 2e \rightleftharpoons Cl^- + H_2O. \qquad (2)$$

In neutral and, especially, in weakly acidic solutions in which ClO^- ions change into HClO, we may expect the following reaction instead of (2):

$$HClO + H^+ + 2e \rightleftharpoons Cl^- + H_2O, \quad (3)$$

Finally, in very acidic solutions in which chlorine is liberated according to reaction (1), the oxidation potential is determined by the electrode process:

$$Cl_2 + 2e = 2Cl^-, \quad (4)$$

It follows from equations (2) and (3) that the oxidation potential must depend on the pH (since it differs in the acidic and alkaline regions) and also on the concentrations of hypochlorite and chlorine ions. In the strongly acid region, where the equilibrium of reaction (1) is sharply shifted to the left, we should expect the oxidation potential to be independent of the pH according to equation (4). The experimental investigation of these relationships will also be dealt with in this paper.

In the first instance measurements were made of the oxidation potentials in freshly prepared solutions of sodium hypochlorite and bleaching powder.

Sodium hypochlorite was prepared by passing chlorine into a solution of sodium hydroxide. The calcium hypochlorite solutions were perfectly transparent and colorless. They were stored in the dark in a dark-glass container. The oxidation potentials were measured with the help of a platinum gauze electrode. The pH of the solutions was determined with an electrode of ES-1 glass (72% SiO_2; 6% CaO; 22% Na_2O). The pH and the oxidation potentials were measured on a lamp potentiometer. The measurements with the glass electrode were accurate to within about 1 mV. A platinum electrode and a potassium chloride-agar siphon, for connection to the calomel electrode, were inserted simultaneously in a beaker closed with a waxed rubber stopper. Through another hole in the stopper was passed the tip of a small buret from which acid or alkali was run into the solution. The second half-element for the measurements was a saturated calomel electrode. All the values of oxidation potentials presented below are expressed in relation to this electrode.

In order to reduce the values of φ to the hydrogen zero point, they must be increased by the value of the potential of the saturated calomel electrode at 18°, i.e. by +0.250 V.

The starting solutions placed in the beaker were either chlorine water or a solution of sodium hypochlorite containing an excess of alkali or a solution of bleaching powder containing an excess of $Ca(OH)_2$. Since hypochlorite solutions only develop a buffering action in the pH range of 8-6, a more detailed study of the effect of pH upon the oxidation potential necessitated buffering of the solutions with boric, acetic or monochloracetic acid.

In the alkaline region the oxidation potential was established slowly at the platinum electrode. A special investigation showed that a constant potential in a solution with pH $\simeq$ 10.5 is only reached after several hours. Consequently measurements carried out in this region were sometimes prolonged for 24 hours or longer. In this case the measurements were considered to be completed when the potential remained constant over a period of several hours. In the neutral and acid regions a steady potential was established more quickly, so that the duration of the pH measurements was then from 30 minutes to a few hours.

In Figures 1 and 2 are plotted the results of the potentiometric titrations. The upper curves characterize the pH change and the lower ones the change in oxidation potentials. Upper and lower curves are quite similar.

The individual portions of these curves correspond to the processes:

$$H^+ + OH^- \rightleftharpoons H_2O, \quad (5)$$

$$ClO^- + H^+ \rightleftharpoons HClO, \quad (6)$$

$$HClO + H^+ + Cl^- \rightleftharpoons Cl_2 + H_2O. \quad (1)$$

The positions of the inflection points of the upper and lower curves coincide on the axis of the abscissas. These inflection points separate from each other the above-noted portions of the titration curves. The identical course of the pH and oxidation potential curves is particularly marked in Figure 3 in which both curves are plotted with an identical scale along the axis of the ordinates (one pH unit corresponds to 58mV of oxidation potential); here the pH values on the ordinates increase from bottom to top, while the values of φ increase from top to bottom.

Analysis showed the content of hypochlorite determined from the titration curve (from the length of the corresponding portion along the axis of the abscissas), agrees with measurements by the iodometric method. The potentiometric titration curves consequently offer the possibility of exact determination of the content of free alkali and active chlorine in a hypochlorite solution, as will be discussed more fully in another paper.

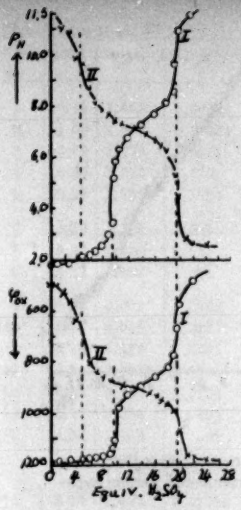

Figure 1. I) Titration of chlorine water with sodium hydroxide; II) titration of sodium hypochlorite with sulfuric acid.

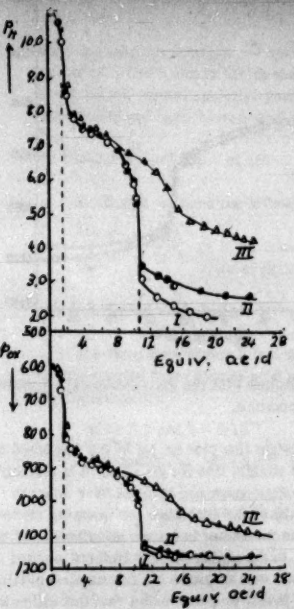

Figure 2. I) Titration with HCl solution; II) titration with monochloracetic acid solution; III) titration with acetic acid solution.

From Figures 1 and 2 and, in particular from Figure 3, it is clear that a definite dependence does actually exist between the oxidation potential and the pH in hypochlorite solutions. This dependence is illustrated in Figure 4. Here are plotted the results of our measurements in hypochlorite solutions (0.0289 N) prepared from chlorine water, and in bleaching powder solutions (0.0293 N). There is substantial agreement between the results of both sets of measurements.

It is interesting to compare the results obtained with the data of other authors. Remington and Trimble [3] give the oxidation potentials measured by them in hypochlorite solutions with the help of a platinum foil electrode. Their solutions were buffered in the pH range of 5.29-8.04 with a phosphate mixture and in the pH range of 8.35-11.59 with a carbonate mixture. Apparently the pH of the solutions was not accurately measured in these experiments.

In this paper it was established that a break in the straight-line dependence occurs in the pH region around 9-8, which the authors attribute to a "solvation" effect associated in their opinion with the use of different buffer systems.

Hisey and Koon [4], who performed measurements in calcium chlorate solutions, show that the rectilinear dependence begins to break down at pH $\leq$ 5.0. Höye [5] made more systematic and accurate measurements of potentials in hypochlorites prepared from chlorine water and presented data which indicate the start of deviation from linearity in a more acidic region (much lower than pH = 5.0).

Our own data reveal the presence of an inflection on the curve in the pH range of approximately 9.3-8.8. Below pH = 8.8 and above pH = 9.3 a rectilinear dependence of the oxidation potential on the pH is observed with the same slope.

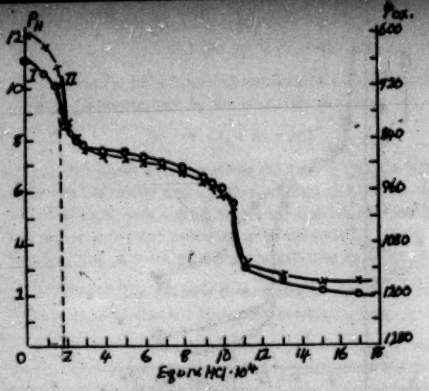

Figure 3. I) Titration with the glass electrode; II) titration of oxidation potentials.

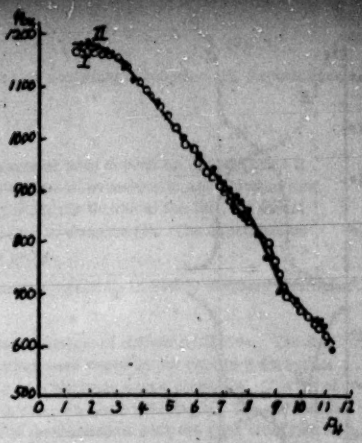

Figure 4. I) Experiments with sodium hypochlorite, II) experiments with sodium hypochlorite.

The straight-line plot for pH ≅ 8,8 lies 55-60 mV higher than the straight line for pH > 9,3. It is scarcely permissible (as Remington and Trimble have done) to attribute the shift of the dependence of φ on the pH from one straight line to another to a specific influence of the buffer system. In the region of pH = 10.5-8.0 we used one and the same borate system but nevertheless obtained an inflection. It will be shown below that this inflection is associated with a change in the character of the equilibrium governing the oxidation potential. Buffering of the solution with acetic and monochloracetic acids permitted a more detailed study of the change of oxidation potential at pH values below 5.0.

As we see, the straight-line course of the dependence of oxidation potential on pH continues down to pH ≅ 3.0. Only at a pH of less than 4 does it begin to change less sharply; finally it becomes substantially constant in agreement with the ideas postulated on the basis of equation (4).

For a study of the effect on the oxidation potential of Cl^-, ClO^- ions and of hypochlorous acid, also of ClO_3^- ions (which might be present in these solutions), measurements were performed in solutions in which the concentration of one of the components was varied while the concentrations of the other components were kept constant. The results of these investigations are enumerated in the table (the experiments were performed at a temperature of 13-15°).

It is clear from the table that in all of the investigated solutions an increase in the concentration of hypochlorite or of hypochlorous acid is accompanied by a rise of oxidation potential. Concerning Cl^- ions, their effect upon the oxidation potential was only detected in experiments carried out with alkaline solutions (pH > 10.0). In all other cases the change of ionic concentration had substantially no effect upon the oxidation potential. This confirms that the inflection on the $\varphi = \varphi(pH)$ curve in the range of pH ≅ 9,3-8,5 is bound up with a change in the character of the equilibrium governing the oxidation potential.

In all the experiments an influence of ClO_3^- ions on the oxidation potential could not be detected.

Analysis of Results

The concentrations of hypochlorite and hypochlorous acid in the solution are governed by the law of mass action; consequently processes (2) and (3) will change into each other according to the change of pH of the solution.

In accordance with these processes the equilibrium oxidation potential is:

$$\varphi = \varphi_0 - \frac{\beta}{2} pH + \frac{\beta}{2} \log \frac{a_{ClO^-}}{a_{Cl^-}}, \qquad (7)$$

TABLE

Expt. No.	pH	C_{Cl^-}	C_{ClO^-}	$C_{ClO_3^-}$	Oxidation potential
Experiments at pH ≅ 10-11					
1	10.95	1.462	0.00089	–	0.480
2	11.09	1.500	0.00483	–	0.538
3	10.99	1.478	0.00853	–	0.549
4	10.86	1.823	0.0890	–	0.597
5	10.75	1.887	0.1780	–	0.611
6	10.28	1.120	0.075	0.0331	0.635
7	10.32	1.120	0.075	0.2791	0.637
8	10.32	1.120	0.075	Saturated $KClO_3$	0.639
9	10.15	0.001	0.0199	–	0.685
10	10.07	0.005	0.0197	–	0.679
11	10.26	0.010	0.0195	–	0.663
12	10.14	0.050	0.0194	–	0.658
13	10.15	0.100	0.0194	–	0.648
14	10.11	0.504	0.0193	–	0.636
15	10.24	0.999	0.0193	–	0.608
Experiments at pH ≅ 8					
16	8.14	1.607	0.00074	–	0.778
17	8.10	1.616	0.00444	–	0.823
18	8.16	1.625	0.00829	–	0.830
19	8.07	1.699	0.0269	–	0.848
20	8.04	1.669	0.1140	–	0.868
21	7.92	0.1490	0.0574	0.0124	0.865
22	8.00	0.1490	0.0593	0.1047	0.861
23	8.07	0.1490	0.0609	Saturated $KClO_3$	0.859
24	8.03	0.0110	0.0084	–	0.831
25	8.05	0.050	0.0085	–	0.825
26	7.96	0.100	0.0082	–	0.830
27	7.96	0.500	0.0082	–	0.833
28	7.96	1.000	0.0082	–	0.831
29	7.91	2.000	0.0080	–	0.831
30	7.91	4.000	0.0080	–	0.828
Experiments at pH ≅ 5-6					
			C_{HClO}		
31	5.37	1.614	0.0088	–	0.999
32	5.36	1.621	0.00472	–	1.010
33	5.30	1.628	0.00931	–	1.022
34	5.20	1.684	0.0445	–	1.043
35	5.18	1.826	0.1180	–	1.061
36	5.03	0.0623	0.0296	0.0153	1.036
37	5.01	0.0623	0.0296	0.0909	1.033
38	5.07	0.0623	0.0296	Saturated $KClO_3$	1.035
39	5.98	0.0100	0.0424	–	0.962
40	6.10	0.0500	0.0418	–	0.958
41	6.10	0.1000	0.0418	–	0.964
42	6.10	0.5000	0.0418	–	0.963
43	6.10	1.1600	0.0418	–	0.964

$$\varphi = \varphi_0 - \frac{\vartheta}{2}\,pH + \frac{\vartheta}{2}\log\frac{a_{HClO^-}}{a_{Cl^-}} \qquad (8)$$

where a_{Cl^-}, a_{ClO^-}, a_{HClO^-} are the concentrations of Cl^-, ClO^-, and $HClO^-$ in the solution; $\varphi_0 - \varphi_0'$ are the normal oxidation potentials of hypochlorite and hypochlorous acid.

$$\vartheta = 2.3\frac{RT}{F} = 0.058 \text{ V at } 18°.$$

In solution we have the following relation:

$$\frac{a_{HClO}}{a_{ClO^-}} = \frac{a_{H^+}}{k} \quad (k \text{ is the dissociation constant of HClO})$$

Hence $\varphi_0 - \varphi_0' = -\frac{\vartheta}{2}\log k = \frac{\vartheta}{2}pk$.

It follows from Figure 3 that the pH of the half-titrated hypochlorous acid is equal to 7.3; consequently:

$$pH = 7.3 \text{ and } k = 5\cdot10^{-8}.$$

Consequently $\varphi_0 - \varphi_0' = 0.212$ V (at 18°)

If the total concentration of active chlorine is b equivalents per liter, then, neglecting the different concentration and activity of the ClO^- ions, we get:

$$\frac{b - a_{ClO^-}}{a_{ClO^-}} = \frac{a_{H^+}}{k} \quad \text{and} \quad a_{ClO^-} = \frac{kb}{a_{H^+} + k},$$

$$a_{HClO} = \frac{ba_{H^+}}{a_{H^+} + k}.$$

Knowing the total concentration of active chlorine (b) in the solution at a given pH, we can calculate φ (the oxidation potential) theoretically for the purpose of comparison with the experimental values.

In the region of pH > 9.3 the measured values of oxidation potential are in complete agreement with equation (7) if we insert the value of $\varphi_0 = 1.267$ V for C_{ClO^-} lying between 0.0297 and 0.0254. This is shown in Figure 5 where the values of φ calculated according to equation (7) are represented by crosses.

Concerning the pH region from 8.8 to 3.5, we see from Figure 5 that the measured values of the oxidation potential do not coincide with the calculated ones (from formulas (7) and (8)) if we use the same value $\varphi_0 = 1.267$ V (broken curve I in Fig. 5).

If, on the other hand, we take for φ_0 a value higher by 55 mV (1.322 V), then we can obtain oxidation potentials substantially in agreement with the experimental values in the pH region from 8.8 to 7.3.

This procedure of course results in a deviation from experimental values at pH > 9.0. With further acidification the calculated values of the oxidation potential (at $\varphi_0 = 1{,}322$) begin to deviate from the experimental results (broken curve II on Fig. 5). Comparison of formulas (7) and (8) shows that with increasing HClO content of the solution the angle of slope of the straight line $\varphi = \varphi(pH)$ is bound to decrease (from 58 to 29 mV per pH unit).

However, experiments have failed to reveal such a change in the slope of the straight line, associated with the transformation of ClO^- into HClO, down to pH $\cong$ 3,5, at which point the change is evidently due to another cause. This permits us to draw the conclusion that the formation of HClO does not influence the oxidation potential. This conclusion is not in accord with the widely held opinion that the oxidizing ability of HClO is greater than that of its salt. Therefore from the absence of an effect of Cl^- upon the oxidation potential and from the presence of an inflection on the $\varphi = \varphi(pH)$ rectilinear plot in the region of approximately 9.3-8.9, it follows that the oxidation potential in the pH range of 9.0-3.5 is not governed by the equilibria on which formulas (7) and (8) are based.

Since the ClO_3^- ions have no effect upon the oxidation potential, it may be inferred that the processes of decomposition of hypochlorites with formation of chlorates, for example:

$$ClO_3^- + 2H^+ + 2Cl^- \rightleftharpoons 2HClO + ClO^-, \qquad (9)$$

likewise do not govern the potentials. The experimental data can likewise not be explained by the fact that the electrode behaves like an oxygen electrode due to the processes:

$$ClO^- \rightleftharpoons Cl^- + \frac{1}{2} O_2. \qquad (10)$$

or

$$HClO \rightleftharpoons H^+ + Cl^- + \frac{1}{2} O. \qquad (11)$$

In this case the electrode potentials ought to be considerably lower than the experimental values (Fig. 5).

An understanding of the equilibria which govern the potential in this pH region calls for further investigation of the properties of hypochlorite solutions.

In the more acidic region (pH < 3.5) chlorine begins to be formed in appreciable amounts in the solution. On this basis we may suggest that the deviations from rectilinearity of the curve (Fig. 5) in the strongly acidic region (pH > 3.0) are due to the influence of the equilibrium of chlorine hydrolysis on the oxidation potential.

Here the oxidation potential of the solution must be determined by the system Cl_2–Cl^-, i.e. the electrode begins to behave like a chlorine electrode.

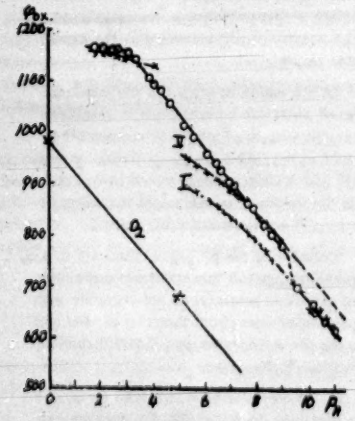

Figure 5. Circles relate to experimental values; crosses to calculated values.

If these considerations are valid, then its potential is:

$$\varphi_{Cl_2/Cl^-} = \varphi^0_{Cl_2/Cl^-} + \frac{\vartheta}{2} \log \frac{a_{Cl_2}}{a^2_{Cl^-}}. \qquad (12)$$

Applying the law of mass action to the hydrolysis of chlorine (I), we get:

$$a_{Cl_2} = k'_h \cdot a_{H^+} \cdot a_{Cl^-} \cdot a_{HClO}, \text{ where } k'_h = \frac{1}{k_h}; \qquad (a)$$

where k_h is the hydrolysis constant of chlorine. According to Yakovkin, at 18°, $k_h = 3{,}75 \cdot 10^{-4}$.

We denote the initial concentrations of hypochlorous acid and chlorides by respectively:

$$a^0_{HClO} = a_{HClO} + a_{Cl_2}, \qquad (b)$$

$$a^0_{Cl^-} = a_{Cl^-} + a_{Cl_2}. \qquad (c)$$

From expressions (a), (b) and (c) we find:

$$a_{Cl_2} = k'_h \cdot a_{H^+} \cdot a_{Cl^-} \cdot (a^0_{HClO} - a^0_{Cl^-} + a_{Cl^-}). \qquad (d)$$

The value of a_{Cl^-} can be obtained by simultaneously solving equations (c) and (d). $\varphi_0 Cl_2/Cl^- = 1.359$ V (in relation to the normal hydrogen electrode).

Since $\varphi_0 Cl_2/Cl^-$ is given for the equilibrium pressure of chlorine equal to one atmosphere, the oxidation potential towards the saturated calomel electrode is:

$$\varphi_{Cl_2/Cl^-} = 1.109 + \frac{\vartheta}{2} \log \frac{P_{Cl_2}}{a^2_{Cl^-}},$$

where P_{Cl_2} is the equilibrium pressure of chlorine at its concentration (activity) in solution equal to a_{Cl_2}.

According to Winkler the solubility of chlorine at a pressure of one atmosphere and a temperature of 20° is 0.7923 g per 100 g water, or 0.105 mole/l.

Taking $\frac{P_{Cl_2}}{a_{Cl_2}} = \frac{1}{0.105}$, we obtain:

$$\varphi_{Cl_2/Cl^-} = 1.109 - \frac{\vartheta}{2} \log 0.105 + \frac{\vartheta}{2} \log \frac{a_{Cl_2}}{a^2_{Cl^-}} V. \qquad (13)$$

The oxidation potentials for values of pH < 4 calculated according to equation (12) are shown by crosses in Figure 5.

We see from Figure 5 that the calculated values are in adequate agreement with the experimental ones. This shows that the platinum electrode actually behaves like the chlorine electrode in the pH region below 3.5.

SUMMARY

1. In hypochlorite solutions with pH > 9.3 the oxidation potential changes with changing concentration of ions of H^+, ClO^- and Cl^-. In this region the potential may be calculated from the formula:

$$\varphi = \varphi_0 - \vartheta pH + \frac{\vartheta}{2} \log \frac{a_{ClO^-}}{a_{Cl^-}}, \text{ where } \varphi_0 = 1.267 \text{ V}.$$

2. In solutions with a pH from 8.5 to 4.0 the dependence of the oxidation potential on the pH is represented by a straight line lying 55-60 mV higher than the straight line obtained in the alkaline region (pH greater than 9.3).

In this region the potential does not change with changing concentration of Cl^- ions in the solution. The oxidation potential in this region is not governed by the equilibria:

$$ClO^- + 2H^+ + 2e \rightleftarrows Cl^- + H_2O \text{ and } HClO + H^+ + 2e \rightleftarrows Cl^- + H_2O.$$

3. An influence of chlorate ions on the oxidation potential in alkaline, neutral and weakly acid regions could not be detected.

4. In solutions with a pH below 3.5 the electrode potential is governed by the equilibrium of chlorine hydrolysis. In this region the electrode behaves like a chlorine electrode.

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REACTIONS OF NITRATES AND NITRITES OF METALS OF THE FIRST AND SECOND GROUPS OF THE PERIODIC SYSTEM IN MELTS

IV. INVESTIGATION OF THE TERNARY SYSTEM OF NITRATES OF LITHIUM, SODIUM AND CADMIUM IN MELTS*

P. I. Protsenko

The reaction between nitrates of the alkali metals and the nitrates of the alkaline earth metals in the fused state was discussed in previous communications [1,2,3,4]. Both in binary and in ternary combinations, the nitrates of the alkali metals alone or in association with the nitrates of the alkaline earth metals do not chemically interact, except in the case of the nitrates of potassium and calcium [1]. In nearly all the cases that we have investigated, simple eutectics or their isomorphous mixtures are formed. In the present communication consideration is given to the character of the interaction of nitrates of lithium and sodium (as the first members of a chief subgroup of Mendeleev's periodic system) with the nitrate of cadmium (as a representative of an adjacent subgroup of the second group of the periodic system).

The paper presents an experimental investigation of the ternary system of the nitrates of lithium, sodium and cadmium in melts, and is a continuation of the author's systematic studies in the field of the chemistry of nitrates and nitrites in the fused state.

The investigation was carried out by the visual-polythermal method of physico-chemical analysis which has been frequently described in the literature, notably by A. P. Palkin and S. D. Gromakov [5].

Binary Systems. 1. The binary system lithium nitrate-sodium nitrate has been investigated by numerous authors: de Cesaris [6], Carveth [7], V. P. Blindin [8], A. P. Palkin and others. According to deCesaris the system contains continuous solid solutions with a minimum. According to Carveth, V. P. Blindin and A. P. Palkin the two salts form a simple eutectic. Our repeated investigations of this system gave results in complete agreement with the data of the last-mentioned authors. Corresponding to the eutectic point is the composition: 43.75 mole % $NaNO_3$ and 56.25 mole % $LiNO_3$, with a melting point of 196°.**

The liquidus curve of the binary system consists of two branches — a gradually descending branch of the primary crystallization of the lithium nitrate and a branch of the primary crystallization of sodium nitrate rising steeply from the eutectic point (Figure 1). The melts of the salts in any given quantitative ratios are transparent with a pale-yellow color, and they crystallize easily.

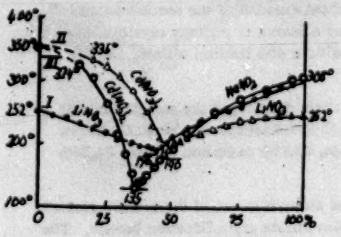

Fig. 1.

2. We have been the first to investigate the system cadmium nitrate-lithium nitrate. This is a system with a eutectic. The liquidus curve comprises two branches — a branch of primary crystallization of cadmium nitrate falling steeply to the eutectic point, and a branch of lithium nitrate crystallization smoothly rising from the eutectic point. The eutectic point corresponds to the composition 46.75% lithium nitrate and 53.25% cadmium nitrate, with a melting point of 190° (Fig.1).

The system was studied in the range from 20 to 100% lithium nitrate. With a smaller content of lithium nitrate the melt decomposes with evolution of nitrogen peroxide.

* Z. A. Milovanova collaborated in the investigation.

** Throughout the paper the composition will be given in equimolar percentages.

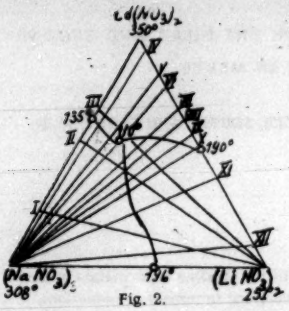

Fig. 2.

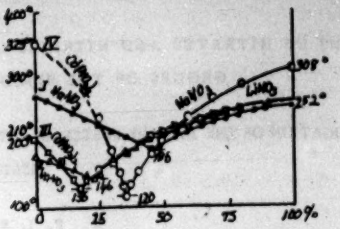
Fig. 3.

3. We have also been the first to investigate the binary system cadmium nitrate-sodium nitrate. The fusion curve of this system consists of two branches — a branch of the primary crystallization of cadmium nitrate descending very steeply to the eutectic point. The eutectic point corresponds to 36% sodium nitrate and 46% cadmium nitrate, with a melting point of 135° (Fig. 1).

The system was investigated in the range from 15% sodium nitrate. As in the previously described system, a lower content of sodium nitrate resulted in decomposition of the melts with evolution of nitrogen peroxide. Melts of salts containing 60-70% cadmium nitrate readily changed into the vitreous state which seriously retarded the development of crystals.

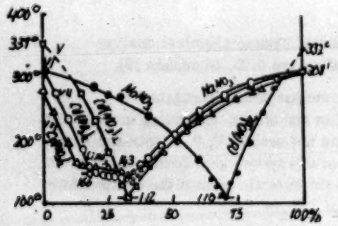
Fig. 4.

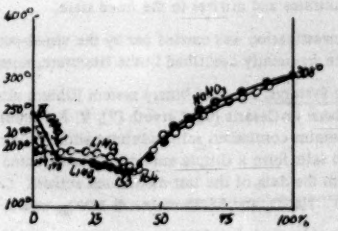
Fig. 5.

Ternary sections. For the purpose of investigation of the liquidus surface of the ternary system, in accordance with the general principles of physico-chemical analysis, 12 sections (Figure 2) were examined.

Section I: 25% $Cd(NO_3)_2$ + 75% $(NaNO_3)_2$ ⟶ $(LiNO_3)_2$. The phase diagram of the section comprises two branches: A branch of primary crystallization of sodium nitrate and a branch of primary crystallization of lithium nitrate (Fig. 3). The transition point corresponds to the composition: 46% lithium nitrate, 13.25% cadmium nitrate, 40.75% sodium nitrate, and a temperature of 168°.

Section II: 55% $Cd(NO_3)_2$ + 45% $(NaNO_3)_2$ ⟶ $(LiNO_3)_2$. The phase diagram of the section consists of two branches: A branch of sodium nitrate crystallization and a branch of lithium nitrate crystallization. The transition point corresponds to the composition: 23% lithium nitrate, 42.25% cadmium nitrate, 34.75% sodium nitrate, and a temperature of 146°.

Section III: 70% $Cd(NO_3)_2$ + 30% $(NaNO_3)_2$ ⟶ $(LiNO_3)_2$. The phase diagram of the section consists of two branches: A cadmium nitrate crystallization branch and a lithium nitrate crystallization branch. The transition point corresponds to the composition: 18% lithium nitrate, 57.5% cadmium nitrate, 24.5% sodium nitrate and a temperature of 136° (Fig. 3).

Section IV: 5% $(LiNO_3)_2$ + 95% $Cd(NO_3)_2$ ⟶ $(NaNO_3)_2$. The section was investigated from 25% sodium nitrate. At a lower content of sodium nitrate, the melt decomposes with evolution of nitrogen peroxide. The

liquidus curve of the section consists of two crystallization branches: A cadmium nitrate and a sodium nitrate branch. The transition point corresponds to the composition: 35.5% sodium nitrate, 3.2% lithium nitrate, 61.3% cadmium nitrate, and a temperature of 120° (Fig. 3). At certain quantitative ratios of the components the melts readily change into a glassy modification.

Section V: 15% $(LiNO_3)_2$ + 85% $Cd(NO_3)_2$ ⟶ $(NaNO_3)_2$. The section was studied from the point corresponding to 15% sodium nitrate. At a lower content of the latter (as in the preceding section) the melts decompose. The liquidus curve of the section consists of two branches, one being the crystallization curve of cadmium nitrate and the other the crystallization curve of sodium nitrate. The transition point is at the composition: 32.5% sodium nitrate, 10.25% lithium nitrate and 57.25% cadmium nitrate and a temperature of 112°. In melts containing from 27.5 to 32.5% sodium nitrate, vitrification is observed (Fig.4).

Section VI: 20% $(LiNO_3)_2$ + 80% $Cd(NO_3)_2$ ⟶ $(NaNO_3)_2$. The phase diagram of the section consists of two branches: A cadmium nitrate crystallization branch and a sodium nitrate crystallization branch. The transition point corresponds to the composition: 29.5% sodium nitrate, 14.5% lithium nitrate, 56% cadmium nitrate and a temperature of 110°. Vitrification was observed in melts with a sodium nitrate content of 25 to 30% (Fig. 4).

Section VII: 30% $(LiNO_3)_2$ + 70% $Cd(NO_3)_2$ ⟶ $(NaNO_3)_2$. The section consists of three crystallization branches: Cadmium nitrate, lithium nitrate and sodium nitrate. The first transition point corresponds to the composition: 18% sodium nitrate, 25% lithium nitrate, 57% cadmium nitrate and a temperature of 156°. The second transition point corresponds to the composition: 32% sodium nitrate, 20.75% lithium nitrate, 47.25% cadmium nitrate and a temperature of 140° (Fig.4). The salt melts on certain portions of the liquidus curve possess a high viscosity and readily change into the vitreous state.

Section VIII: 35% $(LiNO_3)_2$ + 65% $Cd(NO_3)_2$ ⟶ $(NaNO_3)_2$. The section possesses three crystallization branches: cadmium nitrate, lithium nitrate and sodium nitrate. The first transition point corresponds to the composition: 13.5% sodium nitrate, 30.5% lithium nitrate, 56% cadmium nitrate and a temperature of 166°. The second transition point corresponds to the composition: 34% sodium nitrate, 23.5% lithium nitrate, 42.5% cadmium nitrate and a temperature of 143°. Melts of the salts containing between 46 and 55% of cadmium nitrate are very viscous (Fig. 4).

Section IX: 40% $(LiNO_3)_2$ + 60% $(CdNO_3)_2$ ⟶ $(NaNO_3)_2$. The section consists of three crystallization branches: Cadmium nitrate, lithium nitrate and sodium nitrate. The first transition point corresponds to the composition: 9.25% sodium nitrate, 36.5% lithium nitrate, 54.25% cadmium nitrate and a temperature of 178°. The second transition point corresponds to the composition: 36% sodium nitrate, 26.75% lithium nitrate, 38.25% cadmium nitrate and a temperature of 153° (Fig. 5).

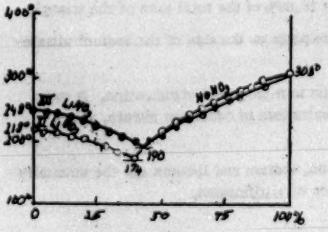

Fig. 6.

Section X: 45% $(LiNO_3)_2$ + 55% $(CdNO_3)_2$ ⟶ $(NaNO_3)_2$. The section has three crystallization branches: Cadmium nitrate, lithium nitrate and sodium nitrate. To the first transition point corresponds the composition: 2.5% sodium nitrate, 44% lithium nitrate, 53.5% cadmium nitrate and a temperature of 189°. To the second transition point corresponds the composition: 37.5% sodium nitrate, 28.25% lithium nitrate, 34.25% cadmium nitrate and a temperature of 164° (Figure 5).

Section XI: 60% $(LiNO_3)_2$ + 40% $Cd(NO_3)_2$ ⟶ $(NaNO_3)_2$. The section possesses two crystallization branches: Lithium nitrate and sodium nitrate. The transition point corresponds to the composition: 40%

sodium nitrate, 36% lithium nitrate, 24% cadmium nitrate and a temperature of 174° (Figure 6). Crystallization proceeded readily throughout the whole course of the section.

Section XII: 90% $(LiNO_3)_2$ + 10% $Cd(NO_3)_2$ ⟶ $(NaNO_3)_2$. The section has two crystallization branches: lithium nitrate and sodium nitrate. The transition point corresponds to the composition: 42.5% sodium nitrate, 52% lithium nitrate, 5.5% cadmium nitrate and a temperature of 190° (Fig. 6).

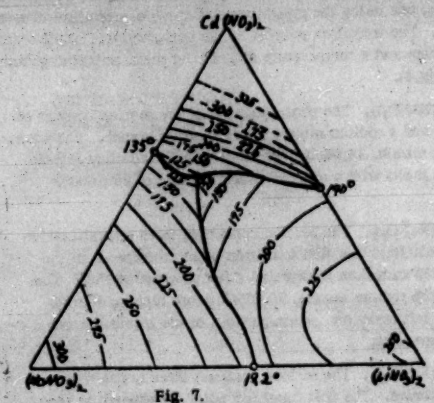

Fig. 7.

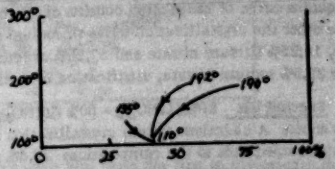

Fig. 8. Projection of the crystallization paths on the side of the sodium nitrate-lithium nitrate triangle

The experimental data for the ternary system are generalized in the projection of the triangular isothermal plots on the phase diagram. The isotherms are drawn through 25° (Fig. 7).

The investigated system of the nitrates of cadmium, sodium and lithium is a system with a simple eutectic, as was to be expected on the basis of the character of the binary systems.

Corresponding to the ternary eutectic point is the composition: 56% mole-% of cadmium nitrate, 14.5% mole-% of lithium nitrate, 29.5% mole-% of sodium nitrate and a melting point of 110° for the ternary eutectic.

The system is characterized by the presence of three crystallization fields:

a) A crystallization field of sodium nitrate comprising 39.12% of the total area of the triangle.

b) A field of crystallization of lithium nitrate with an area of crystallization of 42.5%.

c) A field of crystallization of cadmium nitrate extending over 18.38% of the total area of the triangle.

In Fig.8 is shown the orthogonal projection of the crystallization paths on the side of the sodium-nitrate-lithium nitrate triangle.

A study of this system revealed that the introduction of cadmium ions promoted vitrification. It must be pointed out that vitrification was observed in melts at certain concentrations of cadmium nitrate, which confirms the theory previously advanced by us [1].

Striking features of the ternary system of the nitrates of cadmium, sodium and lithium are the unusually low melting point of the ternary eutectic melt (110°) and the occurrence of vitrification.

SUMMARY

1. The ternary system of the nitrates of cadmium, sodium and lithium was investigated by the visual-polythermal method of physico-chemical analysis.

2. It was established that the system has one invariant point corresponding to the composition: 14.5% mole-% of lithium nitrate, 56% mole-% of cadmium nitrate, 29.5% mole-% of sodium nitrate and a melting point of 110°. It also possesses three fields of crystallization:

a) A cadmium nitrate field extending over 18.38% of the total area of the triangle.

b) A sodium nitrate field (39.12% of the area).

c) A lithium nitrate field (42.5% of the area).

3. It is shown that the largest field of crystallization, contrary to the established views, belongs to the least refractory component – lithium nitrate.

4. The field of formation of a low-melting glass from the nitrates is determined.

5. Two binary systems were studied:

a) Cadmium nitrate-sodium nitrate, which formed a system with the simple eutectic composition: 36% mole-percent of sodium nitrate and 64% mole-percent of cadmium nitrate, with a melting point of 135°.

b) Cadmium nitrate-lithium nitrate, likewise a system with a simple eutectic composition: 46.75% mole-percent of lithium nitrate and 53.25% mole-percent cadmium nitrate, with a melting point of 190°.

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** See Consultants Bureau translation, p. 1509.
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REACTIONS OF NITRATES AND NITRITES OF METALS OF THE FIRST AND SECOND GROUPS OF THE PERIODIC SYSTEM IN MELTS

V. INVESTIGATION OF THE TERNARY SYSTEM OF THE NITRATES OF LITHIUM, POTASSIUM AND CADMIUM IN MELTS*

P. I. Protsenko

In a previous communication [1] it was shown that the nitrates of lithium, sodium and cadmium in melts, both in the binary and ternary systems, do not react chemically with one another but form low-melting eutectics. The substitution of sodium nitrate by potassium nitrate changes the character of the interaction of the components in the melts. Potassium nitrate with cadmium nitrate, as will be shown below, forms a congruent chemical compound $-Cd(NO_3)_2 \cdot 2KNO_3$, which is stable in melts and in the presence of a third component. Examination of this system revealed vitrification which was especially pronounced in the binary system of potassium and cadmium nitrates. The high degree of dispersity of the crystals in melts of the salts at certain concentrations of components and the increasing viscosity under such conditions greatly hindered the performance of the experiment.

Binary systems. 1. The system lithium nitrate-cadmium nitrate was first investigated by the author and has already been described [1].

2. The system lithium nitrate-potassium nitrate was studied by Carveth [2] according to whom the system is a simple eutectic. Corresponding to the eutectic point is the composition: 61.44% mole-% of potassium nitrate and 38.56% mole-% of lithium nitrate and a melting point of 139°. Our investigation confirmed the general character of the system but with slightly different data.

The eutectic point corresponds to the composition: 58% mole-% of potassium nitrate, 42% mole-% of lithium nitrate and a temperature of 120°** (Fig. 1).

As far as we are aware the binary system potassium nitrate-cadmium nitrate has not been described in the literature; we are the first to study it. The system has three crystallization branches; cadmium nitrate descending to the eutectic point (168°); the crystallization branch of the chemical compound $Cd(NO_3)_2 \cdot 2KNO_3$ with a maximum to which corresponds the temperature of 199.5°; and the crystallization branch of potassium nitrate. The cadmium nitrate branch could be followed from the ordinate of the composition corresponding to 20% potassium nitrate and 80% cadmium nitrate to the first eutectic point of 168°. Decomposition of the melt occurred on heating above 250°. The binary system of the nitrates of cadmium and potassium has two eutectics with a maximum. To the first eutectic point corresponds the composition: 37.5% potassium nitrate, 62.5% cadmium nitrate and a temperature of 168°.

To the second eutectic point corresponds the composition: 60% potassium nitrate and 40% cadmium nitrate and a temperature of 175°.

The maximum point, as already indicated above, corresponds to a temperature of 199.5° and the composition: 50% potassium nitrate and 50% cadmium nitrate (Fig. 1).

Investigation of this system involved considerable experimental difficulties since during the entire period of crystallization of cadmium nitrate occurred separation of highly dispersed crystals which led to a rise in viscosity and to vitrification.

Ternary sections. In order to elucidate the character of the interaction of the nitrates of cadmium, potassium and lithium in melts, an investigation of 11 sections was undertaken. From the side of the triangle

* N. M. Shevchenko collaborated in the investigation.

** Throughout the composition will be expressed as mole-equivalent percentages.

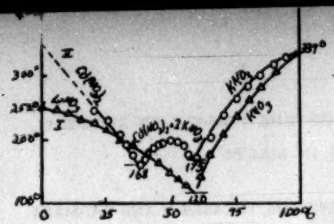

Fig. 1.

I) $LiNO_3 \rightarrow KNO_3$;
II) $Cd(NO_3)_2 \rightarrow (KNO_3)_2$.

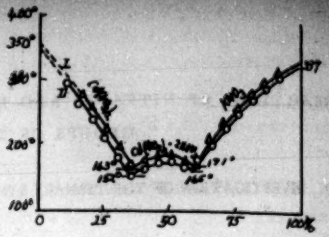

Fig. 2.

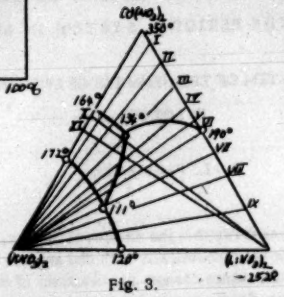

Fig. 3.

I) 95% $Cd(NO_3)_2$ + 5% $Li(NO_3)_2 \rightarrow (KNO_3)_2$;
II) 85% $Cd(NO_3)_2$ + 15% $Li(NO_3)_2 \rightarrow (KNO_3)_2$.

for cadmium nitrate—lithium nitrate to the apex of potassium nitrate were studied the sections I, II, III, IV, V, VI, VII, VIII and IX. From the side of the cadmium nitrate—potassium nitrate triangle to the lithium nitrate apex were studied sections X and XI (Figure 2).

Section I: 95% $Cd(NO_3)_2$ + 5% $(LiNO_3)_2 \rightarrow (KNO_3)_2$. This has three branches of crystallization: cadmium nitrate, descending to the transition point of 163°; the chemical compound $Cd(NO_3)_2 \cdot 2KNO_3$, and potassium nitrate. The temperatures and compositions at the transition points are: 1) 163° and 36.5% potassium nitrate, 3.5% lithium nitrate and 60% cadmium nitrate. 2) 171° and 58.75% potassium nitrate, 2.25% lithium nitrate and 39% cadmium nitrate. Corresponding to the maximum on the curve of the chemical compound is a temperature of 192° (Figure 3). The transition points found by intersection of the crystallization curves were also confirmed experimentally. Along the cadmium nitrate branch there was observed, at certain ratios of components, vitrification which seriously hindered crystallization.

Section II: 85% $Cd(NO_3)_2$ + 15% $(LiNO_3)_2 \rightarrow (KNO_3)_2$. This section has three crystallization branches: cadmium nitrate steeply descending to the transition point (152°); the chemical compound $Cd(NO_3)_2 \cdot 2KNO_3$; and potassium nitrate, likewise steeply rising from the transition point (165°).

This section possesses two transition points and a maximum. The first point is at 152° and has the composition: 34% potassium nitrate, 10% lithium nitrate and 56% cadmium nitrate; the second is at 165° and has the composition: 57.5% potassium nitrate, 6.5% lithium nitrate, and 36% cadmium nitrate.

The transition points were found by intersection of the crystallization curves. The maximum is at a temperature of 179° (Figure 3). Vitrification (which hindered crystallization) was observed on the potassium nitrate branch between the ordinates of the composition ranging from 15 to 34% potassium nitrate. Throughout the remaining extent of the liquidus curve, crystallization of the salts proceeded readily.

Section III: 75% $Cd(NO_3)_2$ + 25% $(LiNO_3)_2 \rightarrow (KNO_3)_2$. This has three crystallization branches: cadmium nitrate, descending in almost a straight line to 134°; the chemical compound $Cd(NO_3)_2 \cdot 2KNO_3$, enclosed between two transition points; and the potassium nitrate branch, steeply rising from 152°.

Section III has two transition points and a maximum point. Corresponding to the first transition point is a temperature of 134° and the composition: 32% potassium nitrate, 17% lithium nitrate, and 51% cadmium nitrate; to the second point corresponds the temperature of 152° and the composition: 56% potassium nitrate, 11% lithium nitrate, and 33% cadmium nitrate.

The temperature of 165° corresponds to the maximum (Figure 4).

Crystallization-hindering vitrification likewise takes place along the course of section III between the ordinates to which corresponds a composition with 10 to 30% potassium nitrate. Separation of the first crystals along the branch of crystallization of the chemical compound and of potassium nitrate was easily observed; the salt melts were transparent and crystallized well.

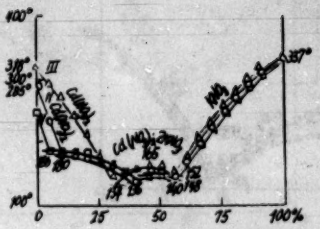

Fig. 4. III) 75% $Cd(NO_3)_2$ + 25% $(LiNO_3)_2$ → $(KNO_3)_2$; IV) 65% $Cd(NO_3)_2$ + 35% $(LiNO_3)_2$ → $(KNO_3)_2$; V) 60% $Cd(NO_3)_2$ + 40% $(LiNO_3)_2$ → $(KNO_3)_2$.

Section IV: 65% $Cd(NO_3)_2$ + 35% $(LiNO_3)_2$ → $(KNO_3)_2$. This is distinguished by four crystallization branches: cadmium nitrate, descending to 180°; lithium nitrate, also smoothly descending to 136°; the chemical compound $Cd(NO_3)_2 \cdot 2KNO_3$; and potassium nitrate. The first transition point corresponds to a temperature of 180° and the composition: 10% potassium nitrate, 31.5% lithium nitrate, and 58.5% cadmium nitrate. The second corresponds to 136° and the composition: 39% potassium nitrate, 22.2% lithium nitrate, and 38.8% cadmium nitrate. The third corresponds to 148° and the composition: 55% potassium nitrate, 16% lithium nitrate, and 29% cadmium nitrate.

The temperature of the maximum point is 158° (Figure 4).

Section V: 60% $Cd(NO_3)_2$ + 40% $(LiNO_3)_2$ → $(KNO_3)_2$. This also has four crystallization branches: cadmium nitrate, lithium nitrate, the chemical compound $Cd(NO_3)_2 \cdot 2KNO_3$, and potassium nitrate. The first transition point corresponds to a temperature of 186° and the composition: 5% potassium nitrate, 39% lithium nitrate, and 57% cadmium nitrate; the second corresponds to 141° and the composition: 40% potassium nitrate, 24% lithium nitrate, and 36% cadmium nitrate; the third corresponds to 140° and the composition: 55% potassium nitrate, 18% lithium nitrate, and 27% cadmium nitrate. The maximum corresponds to a temperature of 148° (Figure 4). The transition points are determined by the intersection of the crystallization curves and were experimentally confirmed. Vitrification was observed along the cadmium nitrate branch.

Section VI: 55% $Cd(NO_3)_2$ + 45% $(LiNO_3)_2$ → $(KNO_3)_2$. This section exhibits three crystallization branches: lithium nitrate, descending to 126°; the chemical compound $Cd(NO_3)_2 \cdot 2KNO_3$, and potassium nitrate. It has two transition points. The first corresponds to a temperature of 126° and the composition: 46% potassium nitrate, 24.5% lithium nitrate, and 29.5% cadmium nitrate; the second to 130° and the composition: 55% potassium nitrate, 20% lithium nitrate, and 25% cadmium nitrate.

The temperature corresponding to the maximum is 143° (Figure 5). Crystallization of the salts proceeded readily throughout the entire section.

Section VII: 45% $Cd(NO_3)_2$ + 55% $(LiNO_3)_2$ → $(KNO_3)_2$. There are two crystallization branches: lithium nitrate and potassium nitrate. The transition point is at 111° and corresponds to the composition: 55% potassium nitrate, 24.75% lithium nitrate, and 20.25% cadmium nitrate (Figure 5). No vitrification was observed throughout the whole of the section.

Section VIII: 35% $Cd(NO_3)_2$ + 65% $(LiNO_3)_2$ → $(KNO_3)_2$. There are two crystallization branches: lithium nitrate and potassium nitrate. The transition point corresponds to the composition: 56% potassium nitrate, 28.5% lithium nitrate, 15.5% cadmium nitrate, and a temperature of 115° (Figure 5). No vitrification was observed on any part of the line, and the salt melts crystallized normally.

Section IX: 20% $Cd(NO_3)_2$ + 80% $(LiNO_3)_2$ → $(KNO_3)_2$. In this case there are two crystallization branches: lithium nitrate and potassium nitrate. The transition point corresponds to the composition: 55% potassium nitrate, 36% lithium nitrate, and 9% cadmium nitrate, and the temperature of 117° (Figure 6). Crystallization proceeded readily throughout the curve.

Section X: 60% $Cd(NO_3)_2$ + 40% $(KNO_3)_2$ → $(LiNO_3)_2$. Two crystallization branches: the chemical compound $Cd(NO_3)_2 \cdot 2KNO_3$ and lithium nitrate. The transition point corresponds to a temperature of 138° and the composition: 33% potassium nitrate, 17.5% lithium nitrate, and 49.5% cadmium nitrate (Figure 6). No vitrification was observed.

Section XI: 55% $Cd(NO_3)_2$ + 45% $(KNO_3)_2$ → $(LiNO_3)_2$. Two crystallization branches: the chemical compound $Cd(NO_3)_2 \cdot 2KNO_3$ and lithium nitrate. The transition point corresponds to the temperature of 140° and the composition: 35.75% potassium nitrate, 20.5% lithium nitrate, and 43.75% cadmium nitrate (Figure 6).

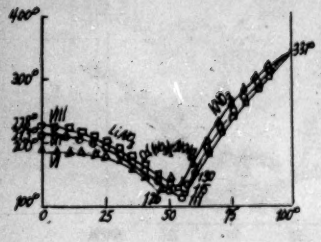

Fig. 5. VI) 55% $Cd(NO_3)_2$ + 45% $(LiNO_3)_2$ → $(KNO_3)_2$; VII) 45% $Cd(NO_3)_2$ + 55% $(LiNO_3)_2$ → $(KNO_3)_2$; VIII) 35% $Cd(NO_3)_2$ + 65% $(LiNO_3)_2$ → $(KNO_3)_2$.

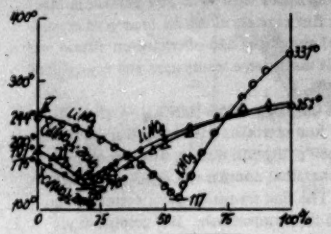

Fig. 6. IX) 20% $Cd(NO_3)_2$ + 80% $(LiNO_3)_2$ → $(KNO_3)_2$; X) 60% $Cd(NO_3)_2$ + 40% $(KNO_3)_2$ → $(LiNO_3)_2$; XI) 55% $Cd(NO_3)_2$ + 45% $(KNO_3)_2$ → $(LiNO_3)_2$.

No vitrification was observed. Section XI confirms the correctness of the course of the lines of common crystallization derived from the data of Sections III, IV, V, VI, VII.

The results of study of the ternary system are generalized in the projection of the triangle of isotherms of the three-dimensional phase diagram. The isotherms are drawn through 25° (Fig. 7).

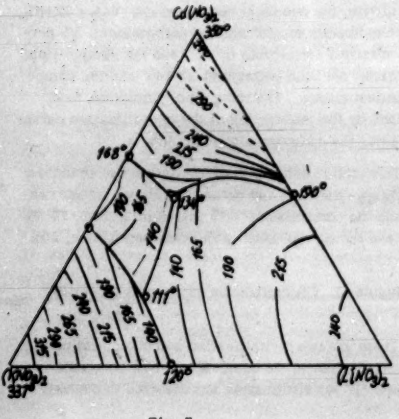

Fig. 7.

Figure 8 shows the orthogonal projection of the paths of crystallization. The composition and temperature of the invariant points obtained by the orthogonal projection of the curves of common crystallization on the cadmium nitrate— potassium nitrate side are in accord with the experimental data.

In the ternary system of the nitrates of lithium, potassium and cadmium, the liquidus surface was investigated. It was established that the system has four fields of crystallization: those of cadmium nitrate, lithium nitrate and the complex compound $Cd(NO_3)_2 \cdot 2KNO_3$. The two binary systems constituting the sides of the ternary system form simple eutectics, while on the third binary system (also forming a side of the triangle) exists the congruent chemical compound $Cd(NO_3)_2 \cdot 2KNO_3$. The composition and temperature of the ternary eutectic points were determined experimentally. This system is characterized by an exceptionally low melting point of the ternary invariant point (a temperature of 111°), and by the presence of a well-defined complex between the nitrates of cadmium and potassium both in the binary system and in the presence of the third component. The formation of the complex compound $Cd(NO_3)_2 \cdot 2KNO_3$ is accompanied by a rise in the viscosity of the salt melts which in turn promotes formation of highly dispersed crystals and hinders observation of the development of the first crystals.

The supercooling of the salt melts, which had been observed with certain concentrations of components, facilitated the formation of a low-melting vitreous mass constituting the simplest nitrate glasses. A similar phenomenon was described by the author when examining the ternary system of the nitrates of calcium, potassium and sodium [3]. Vitrification has also been observed by N.P.Luzhna [4] in a study of the prism of the six salts Na, K, Zn, SO_4, Cl.

The problem of the transformation of certain easily fusible salts into glassy modifications and the associated phenomenon of supercooling have not yet been adequately investigated and further research in this field is required. The treatment of these phenomena in the literature [5,6,7] in our opinion is open to question. From this standpoint our investigation deserves attention both in the theoretical and the practical respect.

SUMMARY

1. The ternary system $Cd(NO_3)_2-(KNO_3)_2-(LiNO_3)_2$ has been studied by the visual-polythermic method of physico-chemical analysis.

2. The ternary system in question is found to belong to the type of ternary systems with two invariant points. Corresponding to the first ternary invariant point is the composition: 32 mole % potassium nitrate, 17 mole % lithium nitrate, 51 mole % cadmium nitrate and a melting point of 134°. To the second invariant point corresponds the composition: 55 mole % potassium nitrate, 24.75 mole % lithium nitrate, 20.25 mole % cadmium nitrate and a melting point of 111°.

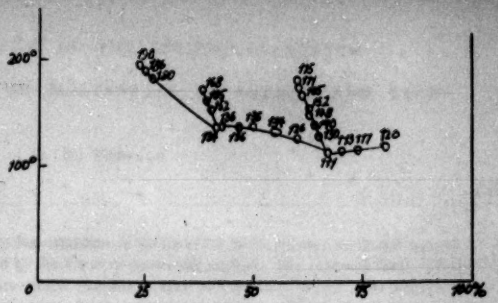

Fig. 8.

3. A study was made of the binary system of the nitrates of cadmium and potassium. This is a system with a maximum point to which corresponds the congruent chemical compound $Cd(NO_3)_2 \cdot 2KNO_3$ with melting point 199.5°.

The first eutectic corresponds to the composition: 38 mole % $(KNO_3)_2$ and 62 mole % $Cd(NO_3)_2$ and a temperature of 168°; to the second corresponds the composition: 60 mole % $(KNO_3)_2$, 40 mole % $Cd(NO_3)_2$ and a temperature of 175°.

4. Potassium nitrate differs from the nitrates of lithium and sodium in forming with cadmium nitrate the complex compound $Cd(NO_3)_2 \cdot 2KNO_3$.

5. It is shown that the introduction of cadmium and potassium ions into salt melts promotes the formation of nitrate glasses of the simplest chemical composition. This is a discovery of undoubted interest.

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THE EQUILIBRIUM IN THE RECIPROCAL SYSTEM OF THE SULFATES AND MOLYBDATES OF SODIUM AND LEAD

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This paper contains the results of an investigation of the fusibility in the ternary reciprocal system of the sulfates and molybdates of sodium and lead by the visual-polythermal method. The salts and their mixtures were melted in a platinum crucible. A resistance-wound crucible furnace of IONKh Alloy No.2* was employed. Temperatures were measured with a platinum – platinum-rhodium thermocouple and with a galvanometer calibrated for the melting points of chemically pure KNO_3, $K_2Cr_2O_7$, Na_2SO_4, KCl, and K_2SO_4. The sodium sulfate was purified by three recrystallizations and had a melting point of 884°; the sodium molybdate was prepared by recrystallization of commercial salt and melted at 698°; lead sulfate and molybdate were prepared by precipitation from solutions of lead nitrate and, respectively, sodium sulfate and sodium molybdate.

TABLE 1

Fusibility of the System $Na_2MoO_4 - PbMoO_4$

No.	$PbMoO_4$ (%)	Temp. of formation of the first crystals
1	0.0	690
2	2.5	721
3	5.0	695
4	10.0	687
5	15.0	681
6	20.0	666
7	22.5	654
8	25.0	644
9	27.5	630
10	30.0	635
11	35.0	676
12	40.0	714
13	45.0	749
14	50.0	784
15	55.0	823
16	60.0	860

TABLE 2

Diagonal Section of $Na_2MoO_4 - PbSO_4$

No.	$PbSO_4$ (%)	Temp. at start of crystallization
1	0.0	690
2	5.0	690
3	10.0	679
4	15.0	666
5	20.0	657
6	25.0	688
7	30.0	758
8	35.0	820
9	40.0	865
10	45.0	898
11	50.0	926
12	55.0	934
13	60.0	943
14	65.0	939
15	70.0	930
16	75.0	899
17	80.0	926

Binary Systems

The binary system sodium sulfate – sodium molybdate, previously described by Boeke [4], was again investigated in our laboratory. The system is characterized by a continuous series of solid solutions which decompose in the solid state under the influence of polymorphic transformations of the components.

The binary system lead sulfate – sodium molybdate has been studied by Ayre and Herms [4]. Limiting solid solutions were observed in the system in the regions adjoining the pure components which form a eutectic at 962° and 42.5% lead sulfate.**

The system of the sulfates of sodium and lead has been studied by Cagliani and Marotta [4]; it is characterized by a simple eutectic at 735° and 47% $PbSO_4$. The results are confirmed by our own experiments (Figure 1).

The binary system of the molybdates of sodium and lead had not previously been studied. Our results are presented in Table 1 and Figure 1. A simple eutectic was observed at 620° and 28% lead sulfate.

The reciprocal system was completely characterized by a study of the diagonal sections and of 10 internal sections. The distribution of the sections is shown in Figure 2.

The diagonal section of $Na_2MoO_4 - PbSO_4$ (Table 2 and Figure 1) has three crystallization branches which intersect at 650° and 23% lead sulfate and at 860° and 79% lead sulfate. The lead molybdate branch has a well-defined maximum at 944° and 60% lead sulfate. The diagonal section of sodium sulfate and lead molybdate clearly exhibits the character of a binary system with a saddle in the region of 50-70% lead molybdate and a eutectic point at 12.5% lead molybdate and 860°.

The fusibility data are presented in Table 3 and Figure 1.

The data for sections I to X are presented in Tables 4-13 and Figures 3-4.

* Institute of General and Inorganic Chemistry.

** Throughout the paper the percentages will be given as mole %.

TABLE 3

Diagonal Section of $Na_2SO_4 - PbMoO_4$

No.	$PbMoO_4$ (%)	Temp. at start of crystallization
1	0.0	884
2	5.0	879
3	10.0	870
4	15.0	861
5	17.5	863
6	20.0	867
7	25.0	875
8	30.0	885
9	35.0	897
10	40.0	909
11	45.0	916
12	50.0	923
13	55.0	928
14	60.0	931
15	65.0	940
16	70.0	960
17	75.0	980
18	80.0	999

TABLE 4

Section I (25% Na_2SO_4, 75% $Na_2MoO_4 + PbSO_4$)

No.	$PbSO_4$ (%)	Temp. at start of crystallization
1	0.0	700
2	5.0	695
3	10.0	691
4	15.0	704
5	20.0	740
6	25.0	782
7	30.0	834
8	35.0	878
9	40.0	906
10	45.0	924
11	50.0	934
12	55.0	936
13	60.0	931
14	65.0	919
15	70.0	895
16	75.0	867
17	80.0	958

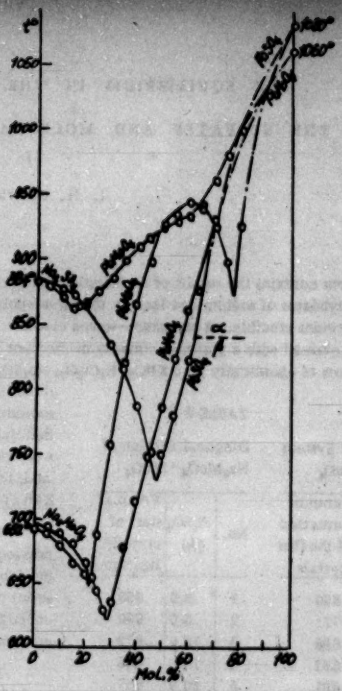

Fig. 1

TABLE 5

Section II (60% Na_2SO_4, 40% $Na_2MoO_4 + PbSO_4$)

No.	$PbSO_4$ (%)	Temp. at start of crystallization
1	0.0	734
2	2.5	732
3	5.0	735
4	7.5	754
5	10.0	770
6	15.0	798
7	20.0	839
8	25.0	870
9	30.0	890
10	35.0	900
11	40.0	900
12	45.0	900
13	50.0	905
14	55.0	895
15	60.0	878
16	65.0	849
17	70.0	845
18	75.0	935

TABLE 6

Section III (75% Na_2SO_4, 25% Na_2MoO_4) + $PbSO_4$

No.	$PbSO_4$ (%)	Temp. at start of crystallization
1	0.0	800
2	2.5	799
3	5.0	811
4	7.5	823
5	10.0	833
6	15.0	849
7	20.0	860
8	25.0	869
9	30.0	880
10	35.0	884
11	40.0	884
12	45.0	878
13	50.0	868
14	55.0	854
15	60.0	814
16	65.0	837
17	70.0	897

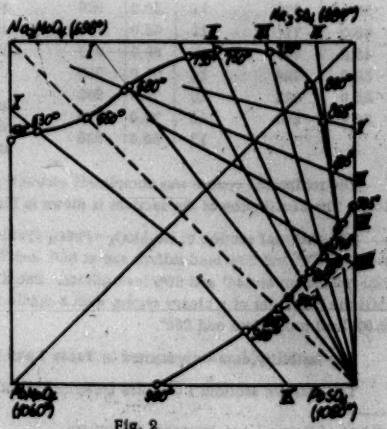

Fig. 2

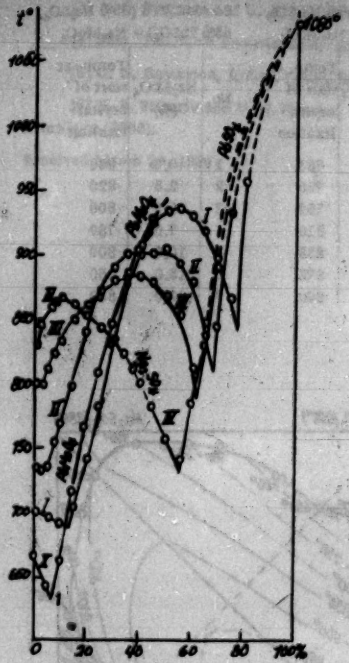

Fig. 3.

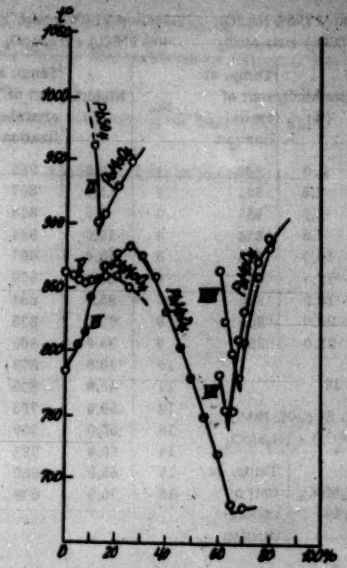

Fig. 4.

From the data of the diagonal and internal sections it has been possible to delineate in a square the reciprocal system of the field of crystallization of the individual salts (Fig. 5). The field of crystallization of lead molybdate occupies the greater part (74.88%) of the square; the field of crystallization of the solid solutions of the sulfate and molybdate of sodium occupy 13.78%; 11.40% in all belongs to the field of crystallization of lead sulfate, of which 9.77% belongs to the α- and 1.63% to the β-modification. One ternary eutectic point was detected in the system at 52% lead sulfate, 3.5% lead molybdate, 44.5% sodium sulfate and 730°; also one binary eutectic point lying on the stable diagonal of $Na_2SO_4 - PbMoO_4$ at 850° and 12.5% lead molybdate.

TABLE 7

Section IV (90% Na_2SO_4, 10% Na_2MoO_4) + $PbSO_4$

No.	$PbSO_4$ (%)	Temp. at start of crystallization	No.	$PbSO_4$ (%)	Temp. at start of crystallization
1	0.0	830	10	35.0	824
2	2.5	845	11	40.0	800
3	5.0	860	12	45.0	782
4	7.5	865	13	50.0	758
5	10.0	867	14	55.0	740
6	15.0	860	15	60.0	785
7	20.0	850	16	65.0	832
8	25.0	845	17	70.0	891
9	30.0	840			

Heat-of-formation data are not available for all of the components, and it is therefore not possible to calculate the thermal effect of the reaction:

$$Na_2SO_4 + PbMoO_4 \rightleftharpoons Na_2MoO_4 + PbSO_4.$$

However, it is clear from the character of the diagram that the equilibrium of the reciprocal reaction is shifted in the direction of linking of ions with radii of the same order of size (larger with larger, smaller with smaller, in accordance with the rules of Gustavson [5] and Beketov [6].)

On the basis of the classification of A. G. Bergman and N. S. Dombrovskaya [1-3] the system is an irreversible reciprocal one, although the presence of a saddle on the stable

TABLE 8

Section V (75% Na_2SO_4, 25% $PbSO_4$) + Na_2MoO_4

No.	Na_2MoO_4 (%)	Temp. at start of crystallization
1	0.0	862
2	2.5	861
3	5.0	857
4	7.5	854
5	10.0	856
6	12.5	856
7	15.0	860
8	20.0	860
9	25.0	850

TABLE 9

Section VI (60% Na_2SO_4, 40% $PbSO_4$) + Na_2MoO_4

No.	Na_2MoO_4 (%)	Temp. at start of crystallization
1	0.0	785
2	5.0	807
3	7.5	813
4	10.0	843
5	15.0	867
6	20.0	879
7	25.0	884
8	30.0	875
9	35.0	860
10	40.0	832
11	45.0	805
12	50.0	780
13	55.0	750
14	60.0	721
15	65.0	680
16	70.0	678

TABLE 10

Section VII (45% Na_2SO_4, 55% $PbSO_4$) + Na_2MoO_4

No.	Na_2MoO_4 (%)	Temp. at start of crystallization
1	0.0	783
2	2.5	755
3	5.0	753
4	7.5	810
5	10.0	833
6	15.0	872
7	20.0	890

TABLE 11

Section VIII (35% Na_2SO_4, 65% $PbSO_4$) + Na_2MoO_4

No.	Na_2MoO_4 (%)	Temp. at start of crystallization
1	0.0	866
2	2.5	826
3	5.0	800
4	7.5	780
5	10.0	809
6	15.0	860
7	20.0	883

TABLE 12

Section IX (20% $PbMoO_4$, 80% $PbSO_4$) + Na_2MoO_4

No.	Na_2MoO_4 (%)	Temp. at start of crystallization
1	0.0	–
2	10.0	960
3	12.5	902
4	15.0	910
5	20.0	930
6	25.0	950

TABLE 13

Section X (80% Na_2MoO_4, 20% $PbMoO_4$) + $PbSO_4$

No.	$PbSO_4$ (%)	Temp. at start of crystallization
1	0.0	665
2	5.0	642
3	10.0	662
4	15.0	717
5	20.0	767
6	25.0	809
7	30.0	846
8	35.0	883
9	40.0	909
10	45.0	927

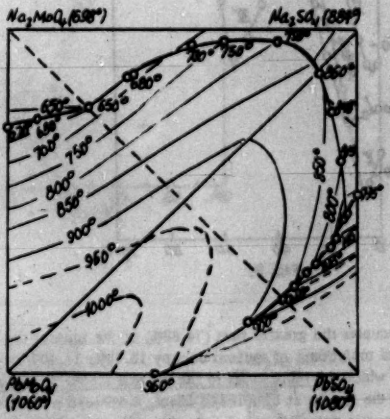

Fig. 5.

Na_2SO_4–$PbMoO_4$ section and the character of the isotherms in the field of crystallization of lead molybdate (displacement of the crest in the direction of lead sulfate) indicate some reversibility of the reaction at high temperatures.

SUMMARY

1. The ternary reciprocal system of the sulfates and molybdates of sodium and lead was investigated by the visual-polythermal method of physicochemical analysis.

2. According to the classification of A. G. Bergman and N. S. Dombrovskaya, the system is of the irreversible-reciprocal type with the stable diagonal Na_2SO_4–$PbMoO_4$.

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THERMODYNAMICS OF THE KETONIZATION OF ETHYL ALCOHOL

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Over certain dehydrogenation catalysts primary alcohols pass through a series of consecutive reactions to form ketones as final products. This so-called ketonization of primary alcohols [1] has chiefly been studied in relation to ethyl alcohol. The reaction mechanism is complicated and is not altogether clear. The most probable scheme is that put forward in 1935 by M. Ya. Kagan, G. D. Lyubarsky and I. A. Sobolev [2], according to which the process successively involves: 1) Dehydrogenation of the alcohol to aldehyde; 2) ester-condensation of the aldehyde; and 3) ketonic cleavage of the ester. The complexity of the ketonization mechanism will also be realized when we recall that even the mechanism of ester formation from alcohols (i.e. the first two stages of the present reaction) has continued until recently to be the subject of investigations and discussions [1,3]. In the temperature range of 250-450° in which ketonization proceeds [1], certain reactions (which appear to be intermediate stages) are substantially reversible, and this fact must be kept in mind during the investigation of the mechanism and kinetics of the reaction. In consequence it is important to have data for the equilibria of the series of reactions taking place under ketonization conditions, for otherwise it would be difficult to demarcate the kinetic and thermodynamic factors when changes occur in the temperature regime.

We are concerned with the equilibria of the following reactions:

$C_2H_5OH \rightleftharpoons CH_3CHO + H_2$ (I) — dehydrogenation of ethyl alcohol,
$2CH_3CHO \rightleftharpoons CH_3COOC_2H_5$ (II) — ester-condensation of acetaldehyde (Tishchenko's reaction),
$2CH_3COOC_2H_5 \rightleftharpoons CH_3COCH_3 + C_2H_4 + CO_2 + C_2H_5OH$ (III) — ketonic cleavage of ethyl acetate,
$3C_2H_5OH \rightleftharpoons CH_3COCH_3 + C_2H_4 + CO_2 + 4H_2$ (IV) — overall reaction of ketonization of ethyl alcohol,
$2C_2H_5OH \rightleftharpoons CH_3COOC_2H_5 + 2H_2$ (V) — reaction of esterification (acidless) of ethyl alcohol,
$3CH_3CHO \rightleftharpoons CH_3COCH_3 + C_2H_4 + CO_2 + H_2$ (VI) — reaction of ketonization of acetaldehyde.

Data for the thermodynamics of reaction (V) were published in 1949 by Vvedensky and co-workers [4]. In the present paper we have calculated the equilibria of the remaining five reactions, using the literature data published in the past ten years (Table 1). In the cases which could be verified, the calculated data agreed with the experimental.

The Reaction of Ethyl Alcohol Dehydrogenation

Since Rideal's data [12], in connection with a study of the equilibrium in the range 150-275°, cannot be considered sufficiently accurate [11], the equilibrium has been calculated on the basis of the third law, using the experimentally determined value of the thermal effect of the reaction: $\Delta H_{298} = 16752$ cal/mole [13].

The calculation, both in the present case and in the others, was performed according to the following scheme:

1. From the data of Table 1 the equation correlating the difference between the heat capacities of the reaction products and the starting products was calculated:

$$\Delta C_p = \Delta\Gamma_0 + \Delta\Gamma_1 T + \Delta\Gamma_2 T^2. \qquad (1)$$

2. From the equation:

$$\Delta H_T = \Delta H_0 + \Delta\Gamma_0 T + \frac{\Delta\Gamma_1}{2} T^2 + \frac{\Delta\Gamma_2}{3} T^3 \qquad (2)$$

the magnitude ΔH_0 was calculated.

For the reaction in question the experimental value of ΔH_{298} was inserted in equation (2); in the remaining cases the value ΔH_{298} determined according to Table 1 was taken.

3. From the equation

$$\Delta Z = \Delta H - T\Delta S \qquad (3)$$

TABLE 1

Thermodynamic Functions of Participants in the Reactions

Compounds (gas)	Heat of formation ΔH^0_{298}	Entropy S_{298}	Equations relating specific heat (C_p) to temp. (°K)	Temp. interval (°K)**
Ethyl alcohol	−56240 [5]	67.26 [6]	$5.5656 + 0.04522T - -0.00001639T^2$ [4]	300-700
Acetaldehyde	−39670 [7]	63.15 [7]	$2.97 + 0.03727T - -0.00001389T^2$*	300-1000
Ethyl acetate	−103444 [4]	90.11 [4]	$2.27 + 0.088T - -0.00003086T^2$ [4]	300-700
Acetone	−57790 [8]	70.3 [9]	$5.37 + 0.048227T - -0.0000151827T^2$ [10]	298-1500
Ethylene	12496 [11]	52.45 [11]	$2.08 + 0.0311T - -0.00001066T^2$ [11]	300-1500
Carbon dioxide	−94052 [11]	51.06 [11]	$5.372 + 0.12404T - -0.00000478T^2$ [11]	300-1500
Hydrogen	0	31.21 [5]	$6.744 + 0.0002774T + + 0.00000001956T^2$ [5]	300-1500

was determined the value ΔZ^0_{298}, ΔS_{298}. Calculation of the value was effected from the data of Table 1.

4. The magnitude of I was calculated by substituting the values ΔZ^0_{298} and ΔH^0_{298}

$$\Delta Z_T = \Delta H_0 - \frac{\Delta\Gamma_0}{0.4343} T \log - \frac{\Delta\Gamma_1}{2} T^2 - \frac{\Delta\Gamma_2}{6} T^3 + IT \quad (4)$$

5. The final equation for the temperature-dependence of $\log K_p$ was obtained by substituting the experimental values in the equation:

$$\log K_p = -\frac{\Delta H_0}{4.573} + \frac{\Delta\Gamma_0}{1.986} \log T + \frac{\Delta\Gamma_1}{2.4573} T + \frac{\Delta\Gamma_2}{6 \cdot 4.573} T^2 - \frac{I}{4.573}. \quad (5)$$

The following was found for reaction (I): $\Delta C_p = 4.1484 - 0.007673T + 0.000003196\ T^2$; $\Delta H_0 = 15714$ cal/mole; $\Delta H^0_{298} = 16637$ cal/mole; $\Delta Z^0_{298} = 8561$ cal/mole; $I = -1.468$.

$$\log K_p = -\frac{3436}{T} + 2.0886 \log T - 0.0008386\ T + 0.0000001166\ T^2 + 0.3210 \quad (6)$$

In Table 2 are presented by comparison the experimental data for $\log K_p$ [12] and those calculated according to equation (6).

TABLE 2

Comparison of $\log K_p$, calculated from equation (6) with the calculated and experimental data of Rideal [12]

t° C	T°K	$\log K_p$ (exp.)	$\log K_p$ (Eq.(6))
150	423	−2.796	−2.651
175	448	−2.322	−2.164
200	473	−1.917	−1.727
225	498	−1.345	−1.334
250	523	−0.635	−0.981
275	548	−0.041	−0.653

The Ester-Condensation Reaction (V.E. Tishchenko's Reaction)

$$2CH_3CHO \rightleftharpoons CH_3COOC_2H_5$$

The expression for the equilibrium constant of this reaction can be derived from the equilibrium constants of the dehydrogenation reaction (I) and of the reaction of esterification in absence of acid (V):

$$K_{p(II)} = \frac{p_{CH_3COOC_2H_5}}{p^2_{CH_3CHO}} = \frac{K_{p(V)}}{K^2_{p(I)}} \quad (7)$$

From this it follows that:

$$\log K_{p(II)} = \log K_{p(V)} - 2 \log K_{p(I)}. \quad (8)$$

On the basis of experimental data A. A. Vvedensky and co-workers [4] proposed the following equation:

$$\log K_{p(V)} = -\frac{1675.7}{T} + 2.33 \log T - 0.0002061\ T + 0.000000084\ T^2 - 2.3929 \quad (9)$$

Combining equations (6) and (9) in accordance with (8), we get:

$$\log K_{p(II)} = \frac{5196}{T} - 1.847 \log T + 0.001471\ T - 0.000000149\ T^2 - 3.0349. \quad (10)$$

* The equation for the specific heat of acetaldehyde was calculated (V.M.) on the basis of the data of Pitzer and Weltner [7] by the method of least squares.

** In this column are listed the temperature ranges put forward for the specific heat equation.

TABLE 3

Comparison of log K_p, calculated from equation (10) with the values calculated from the data of A. A. Vvedensky and co-workers

t° C	T° K	From data of A. A. Vvedensky and co-workers [4]	log K_p from Equation (10)
181	454	4.658	4.140
181	454	4.565	4.140
201.5	474.5	3.662	3.637
201.5	474.5	4.041	3.637

Although there are no papers in the literature on the experimental investigation of the equilibrium of the reaction of ester-condensation of acetaldehyde, for the purpose of comparing the values of log K_p calculated from equation (10) with the experimental data, we may utilize the data given in the paper of A. A. Vvedensky and co-workers devoted to a study of the equilibrium of acidless esterification [4]. Since the aldehyde is an intermediate in the reaction of acidless esterification, its concentration after establishment of equilibrium between alcohol on the one hand and the ester and hydrogen on the other hand will also be an equilibrium concentration. Unfortunately, the concentration of the aldehyde under the conditions described by the authors of the experiments is extremely small (several tenths wt. %), so that even a small absolute error in its determination would introduce a large error into the calculation of the equilibrium constant of reaction (II). The data used in the calculation were taken from those experiments on whose basis the authors derived the equation for the equilibrium constant of the reaction of acidless esterification (Table 3).

Equation (10) permits calculation of ΔH_{298} and ΔZ^0_{298} of the reaction:

$$\Delta H_{298} = -24290 \text{ cal/mole. } \Delta Z^0_{298} = -13980 \text{ cal/mole.}$$

Ketonization of Ethyl Acetate

$$2CH_3COOC_2H_5 \rightleftharpoons CH_3COCH_3 + C_2H_4 + CO_2 + C_2H_5OH \text{ (III)}$$

The following values are found from the data of Table 1: $\Delta H_{298} = 17300$ cal/mole; $\Delta Z^0_{298} = -840$ cal/mole; $\Delta C_p = 12.848 + 0.0726\ T + 0.00001471\ T^2$; $\Delta H_0 = 10114$ cal/mole; I = 47.494.

$$\log K_{p(III)} = -\frac{2212}{T} + 6.469 \log T + 0.007938\ T + 0.0000005358\ T^2 - 10.386. \qquad (11)$$

Ketonization of Ethyl Alcohol

$$3C_2H_5OH \rightleftharpoons CH_3COCH_3 + C_2H_4 + CO_2 + 4H_2 \text{ (IV)}$$

$\Delta H_{298} = 35374$ cal/mole; $\Delta Z^0_{298} = 6497$ cal/mole; $\Delta C_p = 23.101 + 0.06882\ T + 0.00001933\ T^2$; $\Delta H_0 =$

$= 25259$ cal/mole; I = 78.225.

$$\log K_{p(IV)} = -\frac{5523}{T} + 11.632 \log T + 0.007525\ T + 0.0000007041\ T^2 - 17.325 \qquad (12)$$

Ketonization of Acetaldehyde

$$3CH_3CHO \rightleftharpoons CH_3COCH_3 + C_2H_4 + CO_2 + H_2 \text{ (VI)}$$

$\Delta H_{298} = -14336$ cal/mole; $\Delta Z^0_{298} = -18977$ cal/mole; $\Delta C_p = 10.656 + 0.09183\ T + 0.00000974\ T^2$;

$\Delta H_0 = -21679$ cal/mole; I = 83.649.

$$\log K_{p(VI)} = \frac{4741}{T} + 5.366 \log T + 0.01004\ T + 0.0000003649\ T^2 - 18.292 \qquad (13)$$

In Table 4 are presented the values of log K_p of reactions I-VI calculated from the above equations.

The calculations enable the following conclusions to be drawn:

1) The mechanism of the ketonization of ethyl alcohol proposed by M. Ya. Kagan and co-workers is thermodynamically probable in all its stages.

2) In the temperature range 250-450° (in which the ketonization was effected [1]) the reactions of ketonization of alcohol, aldehyde and ester are substantially irreversible.

3) The temperature of 250° is not the bottom limit for the ketonization of alcohol, aldehyde and ester. By choosing suitable catalysts it is possible to effect these reactions at lower temperatures.

TABLE 4

log K_p of Reactions I-VI calculated from the Respective Equations

Reaction	250°C	300°C	350°C	400°C	450°C
$C_2H_5OH \rightleftharpoons CH_3CHO + H_2$ (I)	−0.981	−0.357	0.165	0.611	0.995
$2CH_3CHO \rightleftharpoons CH_3COOC_2H_5$ (II)	2.610	1.733	1.003	0.385	−0.143
$2CH_3COOC_2H_5 \rightleftharpoons CH_3COCH_3 + C_2H_4 + CO_2 + C_2H_5OH$ (III)	7.259	8.321	9.295	10.205	11.071
$3C_2H_5OH \rightleftharpoons CH_3COCH_3 + C_2H_4 + CO_2 + 4H_2$ (IV)	7.775	9.663	11.277	12.747	14.102
$2C_2H_5OH \rightleftharpoons CH_3COOC_2H_5 + 2H_2$ (V)	0.649	1.020	1.333	1.605	1.846
$3CH_3CHO \rightleftharpoons CH_3COCH_3 + C_2H_4 + CO_2 + H_2$ (VI)	10.701	10.652	10.706	10.846	11.052

4) In kinetic studies of the ketonization reaction, account should be taken of the reversibility of reactions I (dehydrogenation of alcohol), II (ester-condensation of aldehyde) and III (acidless esterification of alcohol). Knowledge of the velocity constants of these reactions provides the possibility of determination of the distance of the reacting system from the equilibrium point, and of ascertaining which reaction governs the velocity of the overall reaction.

SUMMARY

On the basis of thermodynamic data published in the literature of the past ten years, equations are derived for the temperature dependence of the logarithm of the equilibrium constants of the following reactions: 1) Dehydrogenation of ethyl alcohol; 2) ester-condensation of acetaldehyde (V. E. Tishchenko's reaction); 3) ketonization of ethyl acetate; 4) ketonization of ethyl alcohol; 5) ketonization of acetaldehyde.

It is shown that in the experimentally established temperature range of ketonization of 250-450°, the last three reactions are substantially irreversible.

The author expresses his sincere gratitude to A. A. Vvedensky for a number of valuable observations.

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* See Consultants Bureau translation, p. 1119.

** See Consultants Bureau translation, p. 1087.

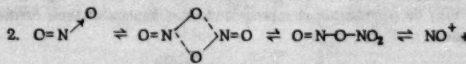
THE MECHANISM OF REACTION OF NITROGEN DIOXIDE WITH AROMATIC HYDROCARBONS

A. I. Titov

The problem, important in itself, of the mechanism of the reaction of nitrogen dioxide with the nuclei of aromatic compounds has acquired even greater theoretical significance following our discovery that the nitration of aromatic compounds (including hydrocarbons) by nitric acid, up to a concentration of acid characteristic of each substance, proceeds through intermediate interaction with nitrogen dioxide [1]. The clarification of the process is made difficult by a series of factors, namely: the complexity of the molecular composition of nitrogen dioxide itself, the formation in the sphere of reaction of other oxy compounds of nitrogen (NO, N_2O_3, HNO_2, HNO_3, etc), the presence of free oxygen, the diversity of products formed, and the inadequacy with which they have been studied.

Among the experimental data on the action of nitrogen dioxide on aromatic hydrocarbons, great interest is presented by the numerous observations of the smooth transformation of naphthalene into α-nitronaphthalene. In contrast to this, Wieland [2] found that the heating in a sealed tube at 80° of an equimolecular mixture of benzene and N_2O_4 gave, apart from nitrobenzene, a considerable amount of trinitrobenzene and picric acid. Attention is also merited by the work of Meisenheimer [3] and Schmidt [4] on the formation of addition products of oxides of nitrogen with anthracene and phenanthrene in the 9,10-position.

In our opinion nitrogen dioxide constitutes an equilibrium system of the following components:



(A) (B) (C) (D) (1)

The dimeric form (B) is stable in a nonpolar medium at low temperatures; rise of temperature and of the degree of dilution leads to breakdown to molecules of NO_2. An increase in the polarity of the medium and of its dissociative power will favor the development of the nitrosyl-nitrate form (C) and of its ionization with formation of the nitrosyl cation NO^+ (D); the latter process should be very strongly promoted by the presence of hydrogen or "aprotonic" acids which combine with the nitrate ion, for example, very concentrated nitric acid:

$$N_2O_4 \rightleftarrows NO^+ + NO_3^-$$

$$NO_3^- + H^+ \longrightarrow HNO_3 \text{ or } NO_3^- + HNO_3 \rightleftarrows NO_3^- \ldots HNO_3. \qquad (2)$$

Reaction of N_2O_4 with sulfuric acid and similar strong acids leads to formation of the nitrosyl cation NO^+ and the nitronium cation NO_2^+.

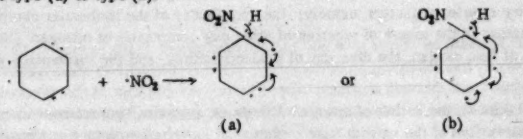
On the basis of the above facts, it is assumed in our theory that the active agent during nitration in a nitric acid medium is the nitrosyl cation NO^+, in sulfuric acid it is the nitronium cation NO_2^+, and in a nonpolar medium it is predominantly the monomer of nitrogen dioxide. All of these agents possess a low electron potential ($P_{NO\dot{X}}$ [1]) and accessibility of their electrophilic nitrogen atoms.

We have now collected a good deal of evidence in support of our theory that, as a rule, the initial stage in the interaction of oxides of nitrogen with aromatic hydrocarbons in large excess is the reaction with monomeric nitrogen dioxide. In agreement with the above theory we observed (see Experiment 1) a very large increase in the overall yields of products of reaction of the same quantity of nitrogen dioxide with benzene with increasing amount of hydrocarbon. The yield-improving effect of dilution, which is contrary to theory, may be accounted for by the decline in the inhibiting action of nitric oxide due to the displacement of the equilibrium to the left:

$$NO + NO_2 \rightleftarrows N_2O_3. \qquad (3)$$

Further evidence that the active agent is NO_2 is provided by our observations on the possible realization of the reaction at 100-150° and with high dilution with the hydrocarbon, i.e. under conditions of substantially complete dissociation of N_2O_4 (Experiment 3). In harmony with our conclusion we observed a sharp acceleration of the reaction of nitrogen dioxide with benzene when saturated with oxygen (Experiment 2) which had the effect of breaking the bond of NO_2 with nitric oxide (see Equation 3). In this case, however, the manifestation was also possible of the specific action of the initial products of reaction of oxides of nitrogen with molecular oxygen.

According to our theory the reaction of NO_2 with the benzene ring leads to formation of the radical , whose structure to a first approximation (allowing for the homolytic conjugation) can be represented by a structure of type (a) or type (b):

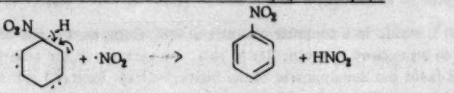


(4)

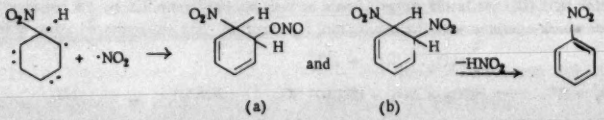
(the dots signify associated electron pairs participating in the conjugation). Heterolytic conjugation also no doubt takes place at the same time.

Among the products of reaction of nitrogen dioxide with benzene, we succeeded in separating nitrobenzene, m-dinitrobenzene, symm.-trinitrobenzene, p-dinitrobenzene, 2,4-dinitrophenol, and picric and oxalic acids. In the light of the foregoing exposition and of the inertness of nitrobenzene towards nitrogen dioxide under our experimental conditions, it may be permissible to represent the mechanism of their formation from the radicals (4) by the following schemes:

1. Formation of Nitrobenzene by Schemes (5) and (6):

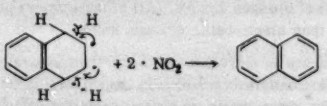


(5)



(6)

Detachment of partly atomic hydrogen according to scheme (5) corresponds to the first stage of nitration of paraffins [5] R–H + · NO_2 ⟶ R + HNO_2; but in this case instead of a free radical there is formed a stable molecule which also promotes the rapid course of the reaction without expenditure of energy of activation. This reaction is analogous to the dehydrogenation of hydroaromatic compounds by NO_2, for example dihydronaphthalene:

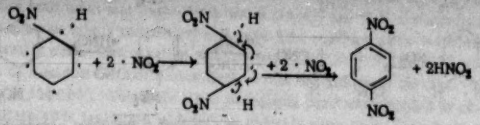


(7)

The ease of realization of such reactions reflects the strong tendency of these compounds to form aromatic nuclei (cryptoaromatic state).

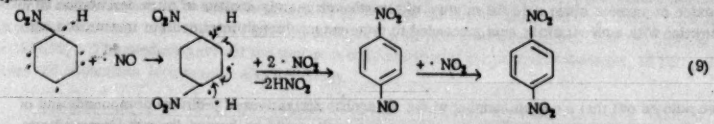
The formation of a mononitro derivative proceeds especially smoothly during reaction of NO_2 with naphthalene. When NO_2 reacts with anthracene and phenanthrene the process takes place according to scheme (6) and stops at stage (6a).

2. Formation of p-Dinitrobenzene:



(8)

It proceeds in a similar manner to the dehydrogenation of dihydronaphthalene in accordance with equation (7). It is quite likely that a portion of the p-dinitrobenzene is formed through the stage of addition of nitric oxide to the radical of (5), dehydrogenation of the adduct and oxidation of the resultant p-nitrosobenzene to the dinitro compound:

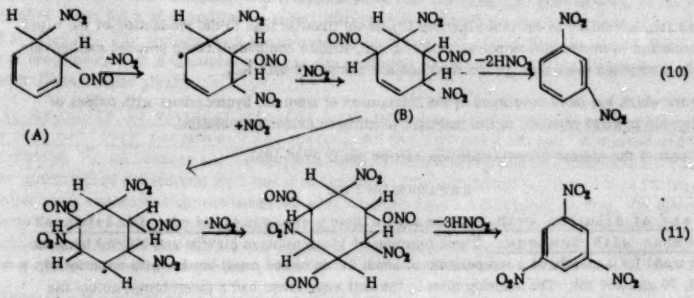


(9)

The still unisolated o-dinitrobenzene is undoubtedly also formed by this route.

3. Formation of m-Dinitrobenzene and symm.-Trinitrobenzene.

These are undoubtedly formed as a result of further addition of NO_2 to the intermediate product, cyclohexadiene [see, for example, schemes (6) and (8)] followed by cleavage of the elements of nitrous acid:



(10)

(A) (B)

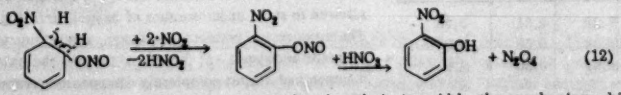
(11)

(C)

Some of our observations and those of Puranen [6] indicate the possible appearance among the reaction products of adducts of types (B) and (C).

4. Formation of Nitrophenols

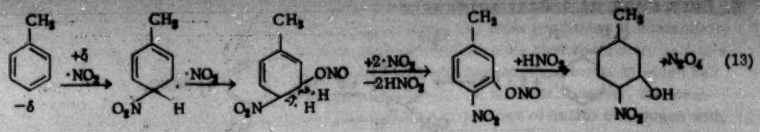
This proceeds through the stage of dehydrogenation of adducts (A), (B) and (C) [see equations (10) and (11)], for example according to the scheme:



(12)

The resultant nitrophenol is converted into dinitrophenols and picric acid by the mechanism which had been clarified in the preceding paper [1]. Dehydrogenation of the adducts (B) and (C) leads respectively to dinitrophenol and picric acid.

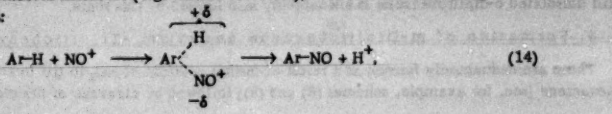
On the basis of the proposed mechanism the reaction of toluene with nitrogen dioxide should be expected to yield nitro derivatives of m-cresol, while in the case of the reaction of NO_2 with chlorobenzene we should expect nitro derivatives of m-chlorophenol, as can be seen, for example, from the following simplified scheme:



(13)

We have actually succeeded in demonstrating that trinitro-m-cresol is the chief component of the mixture of nitrocresols formed in the reaction of NO_2 with toluene, whereas the predominating product in the mixture of nitrocresols resulting from the nitration of toluene with strong nitric acid or sulfuric-nitric mixture is dinitro-p-cresol, probably in admixture with dinitro-o-cresol. We have likewise shown that in the nitration of chlorobenzene with nitrogen dioxide or aqueous nitric acid the mixture of nitrophenols mainly consists of nitro derivatives of m-chlorophenol; nitration with aqueous nitric acid proceeded to some extent through intermediate interaction with NO_2.

It must be pointed out that a certain number of the mononitro derivatives of p-dinitro compounds and of nitrophenols, including also anomalous members (e.g. trinitro-m-cresol), could be formed through intermediate formation of nitroso compounds:



(14)

whose transformation, according to our investigations [3], could likewise lead to the production of the cited compounds. Formation of m-dinitro compounds and of symm.-trinitro compounds could proceed exclusively by the previously mentioned route through the intermediate compound with NO_2.

The theory which has been developed of the interaction of aromatic hydrocarbons with oxides of nitrogen is applicable in large measure to the reactions of nitrogen oxides with olefins.

A large part of the present investigation was carried out in 1940-1941.

EXPERIMENTAL

1. Effect of dilution with hydrocarbon upon the yield of the reaction of nitrogen dioxide with benzene. Three mixtures of 10 ml nitrogen dioxide and 200 ml benzene were allowed to stand for 4 months at a temperature of about 20° in closed small bottles with volumes of, respectively, 40, 70 and 230 ml. The reaction mass in the first experiment had a green-brown color; the greenish tinge due to N_2O_3 in the second experiment was somewhat weaker, while in the third it was scarcely noticeable. A little oxalic acid separated out in each experiment. Picric acid was determined as potassium picrate which was obtained by treating the reaction mass with 10 ml of 10% $KHCO_3$ solution. The total yield of nitro- and polynitrobenzenes was determined by fractionation of the benzene in vacuum while heating on the water bath. Yields of the various products are summarized in the following table.

Expt. No.	Vol. of benzene	Yield		
		$H_2C_2O_4$ in g	picrate in g	nitro derivatives in g
1	20	0.29	0.31	0.26
2	50	0.34	0.60	0.87
3	200	0.68	0.95	2.6

2. Effect of presence of oxygen upon the interaction of nitrogen dioxide with benzene. A mixture of 100 ml benzene and 9.6 g nitrogen dioxide was allowed to stand under pressure of oxygen from a gasholder. The mixture was periodically shaken, sometimes while passing a stream of oxygen. At the end of 20 days the oxides of nitrogen had almost completely disappeared (compare expt. 4). The reaction mass was worked up to give 2.9 g picrate and 14.8 g nitrobenzene, the latter distilling without decomposition and almost without residue at 205-208°.

3. Interaction of nitrogen dioxide with benzene at 100° in sealed tubes with considerable dilution with hydrocarbon. Isolation of symm.-trinnitrobenzene. Into each of two sealed tubes (capacity about 100 ml) was charged 2 ml nitrogen dioxide and 15 ml benzene. The duration of heating in a horizontal water bath was 4 hours. Considerable pressure was manifested on opening

the tubes. Each of them was found to contain about 9.4 ml of aqueous layer with specific gravity 1.24. The hydrocarbon layer from both tubes was washed with water (10 ml) and then extracted with 20 ml of 5% caustic alkali solution. The aqueous layers and the extracts gave 0.14 g residue after evaporation. This residue consisted mainly of oxalic acid. The alkaline solution was acidified with hydrochloric acid and steam-distilled with a small volume of liquid in the distillation flask. From the residue in the flask (32 ml) was separated 0.29 g picric acid with m.p. 104-107°. This gave a rise in melting point when heated in admixture with an authentic specimen. The distillate after saturation with sodium chloride was extracted with ether. From the ether extract was obtained 0.05 g of 2,4-dinitrophenol, melting at about 105°.

The excess of hydrocarbon was distilled off in vacuum from the benzene layer after washing with water. The residue (1.24 g) was steam-distilled. From the distillate was separated about 1 g of liquid consisting mainly of nitrobenzene. The solid residue (0.15 g) from the distillation flask was crystallized from alcohol. The crystals obtained melted at 117-119°; in admixture with pure symm.-trinitrobenzene the melting point was 121-122°. The product gave all the reactions characteristic of symm.-trinitrobenzene, in particular the intense red coloration with caustic alkali solution.

4. Reaction of nitrogen dioxide with benzene at the ordinary temperature and pressure. Isolation of p-dinitrobenzene. A mixture of 500 ml benzene, 20 ml nitrogen dioxide and 2.1 g sodium nitrite was left to stand for six months (the cork was loosely inserted); a portion of the nitrogen dioxide did not enter into reaction. Extraction of the reaction mass with sodium bicarbonate solution gave 5.8 g picric acid; the caustic alkaline extract, following acidification and steam-distillation, yielded 0.5 g of 2,4-dinitrophenol with m.p. 106-109°. After distillation of the benzene (24.3 g) the residue was composed mainly of nitrobenzene. Steam-distillation of later fractions (i.e. after removal of the nitrobenzene) gave about 0.8 g of crystalline material. This crystallized from alcohol in the form of needlets melting at 168-170°. The melting point was elevated after mixing with pure p-dinitrobenzene. The identity of the product with p-dinitrobenzene was also confirmed by its conversion into p-nitrophenol when boiled with dilute caustic alkali.

5. Reaction of nitrogen dioxide with benzene at a temperature of 50-55° and at the ordinary pressure. Separation of m-dinitrobenzene. A mixture of 20 ml nitrogen dioxide, 930 ml benzene and 5 g anhydrous calcium nitrate was heated in a flask beneath a reflux condenser (ground-glass connection) for a period of 100 hours. The experiment was spread over 20 days. The reaction mass was worked up with water and after filtration gave 1.8 g calcium oxalate. On subsequent stirring with 100 ml of 10% potassium bicarbonate solution, a picrate was precipitated which yielded 4.6 g picric acid, m.p. 111-115°. Acidification of the mother liquor from the picrate followed by steam-distillation gave 0.35 g crystalline 2,4-dinitrophenol.

Benzene was distilled off in vacuum from the hydrocarbon layer. By means of combined distillation in steam and in vacuum the residue (6.95 g) gave 5.1 g nitrobenzene and 2.1 g m-dinitrobenzene in admixture with a little p-dinitrobenzene. Two crystallizations of the mixture of dinitrobenzenes (m.p. 70-100°) from alcohol gave a product melting at 82-84° which exhibited melting point elevation when mixed with pure m-dinitrobenzene. The residue of material nondistillable in steam (about 1.3 g) gave a definite reaction for symm-trinitrobenzene but the pure product could not be isolated.

In a similar experiment whose conditions were not precisely defined, steam-distillation of the mixture of dinitrobenzenes yielded a product with m.p. of about 130° from which p-dinitrobenzene was crystallized (from alcohol) with m.p. 161-165°.

6. Action of nitrogen dioxide on toluene in presence of oxygen. Isolation of trinitro-m-cresol and dinitro-p-cresol. A mixture of 2 l toluene, 10 ml nitrogen dioxide and 10 ml calcium nitrate was stood in a bottle under oxygen pressure with occasional shaking. Further addition was made of 6 ml nitrogen dioxide every two days. About 1.5 ml oxygen was absorbed each day; in addition 0.5 l oxygen was expended in driving out accumulated nitrogen and residual gases. After standing for 8 days the reaction mass was treated with water, and then, in succession, with 100 ml of 20% $KHCO_3$ solution and the same volume of 20% K_2CO_3 solution. The extraction with bicarbonate resulted in precipitation of 0.12 g crystals which on further treatment with hydrochloric acid yielded a substance melting at 85°. This was not examined closely. Inspissation of the solution on the water bath gave 1.05 g yellow crystalline salt. Acidification of the solution of the latter gave 0.8 g pure trinitro-m-cresol with m.p. 105° and depressing the melting point of an authentic specimen.

From the carbonate extract was obtained 0.26 g red crystalline precipitate which was worked up with acid to give dinitro-p-cresol, m.p. 80.5° (no depression of mixed melting point). Acidification of the mother liquors of both extracts led to the isolation of about 1 g of a liquid mixture of nitrocresols. The reaction mass was found to contain (using the previously described procedure [5]) 0.9 g of a mixture of o- and p-nitrotoluenes, over 50 g of methyl-substituted products (7 g phenylnitromethane, 29.6 g benzyl alcohol and its ethers, 7 g benzaldehyde, 2 g benzoic acid and 8 g of so-called residual oil). We have previously discussed the mechanism of formation of the latter [5, 7].

SUMMARY

1. The yield from the reaction of nitrogen dioxide with benzene is found to increase proportionally with the dilution of the hydrocarbon. Saturation of the mixture with oxygen strongly accelerates the reaction.

2. From the reaction products were isolated nitrobenzene, m- and p-dinitrobenzenes, symm.-trinitrobenzene, 2,4-dinitrophenol, 2,4,6-trinitrophenol, and oxalic acid.

3. It is shown that dinitro- and trinitrobenzenes are formed when the reaction is performed in sealed tubes at 100-150° with high dilution of the nitrogen dioxide with benzene, and also at the ordinary pressure and temperature.

4. The previously advanced theory of the interaction of nitrogen dioxide with aromatic hydrocarbons is developed. According to this, the primary stage of the reaction in a nonpolar medium is the intermediate formation of the product of addition of the electrophilic and radical-like molecule of NO_2 to the benzene ring. Transformations of the resultant radical under nitration conditions lead to the observed reaction products.

5. In conformity with the theory it is found that the main component of the mixture of nitrocresols resulting from the reaction of nitrogen dioxide with toluene is trinitro-m-cresol, while with chlorobenzene the main product is trinitro-m-chlorophenol.

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* See Consultants Bureau translation, p. 467.

THE MECHANISM OF NITRATION OF AROMATIC COMPOUNDS WITH NITRIC ACID

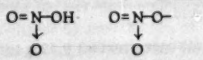
III. NITRATION OF BENZENE WITH DILUTE NITRIC ACID

A. I. Titov and A. N. Baryshnikova

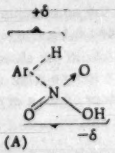
In our previous communications [1,2] it was shown that the nitration of aromatic compounds with nitric acid up to a certain concentration of the latter (characteristic for each compound) proceeds through intermediate interaction with nitrogen dioxide. In these cases the nitric acid merely serves as a source of nitrogen dioxide and as a medium for its regeneration from lower oxides. The strength of the nitric acid required for development of the catalytic action of nitrogen dioxide upon nitration is very high (> 80%) for highly nucleophilic aromatic substances such as naphthalene and phenolic ethers. Preliminary experiments have shown that in the nitration with nitric acid of benzene itself and of compounds with still lower reactivity, the accelerating effect of nitrogen dioxide is only manifested at relatively low concentrations of the order of 20-30% and lower. The theory of these phenomena has been considered in the previous communications [1,2].

On the other hand we have found [3] that during the action of nitrogen dioxide on benzene at temperatures of 100° and higher, even at very high dilution with the hydrocarbon, the reaction product consists of approximately equal amounts of symm.-trinitrobenzene, picric acid and nitrobenzene. These data led us to the conclusion that the principal products of reaction of dilute nitric acid with benzene must be polynitro derivatives – trinitrobenzene and picric acid. Experiment has fully confirmed this paradoxical conclusion. Trinitrobenzene was formed also when nitration was carried out with more concentrated nitric acid in presence of nitrogen dioxide, but in these cases its formation was accompanied to a greater or lesser degree by "normal" nitration of benzene, leading exclusively to nitrobenzene and minute amounts of nitrophenols. In conformity with our theory the minimization of normal nitration was promoted by addition of nitrates. The mechanism of interaction of benzene with oxides of nitrogen has been considered in our recent paper [3], and the theory of "normal" nitration has also been recently discussed [2], the latter in more detail in another paper [4]. In a general form the results of the present investigation have already been published [5].

The causes of the extreme difficulty of nitration of the aromatic nucleus with molecules of nitric acid have been previously discussed. The following ideas are put forward to supplement our earlier explanations. The molecule of nitric acid, and still more the nitrate ion:



is conspicuously stable thanks to the conjugation of the π- and p-orbitals, interaction of the orbitals necessitating parallelism between the axes of the respective electrons, for otherwise the atoms of nitrogen and oxygen would be arranged in the same plane. In the development of the transition complex (A):



(A)

the arrangement of the atoms around the nitrogen will deviate from the planar distribution and will approach the tetrahedral arrangement; this will upset the conjugation and lead to an increased activation energy. These hindrances, likewise steric hindrances, are absent during formation of the transition complexes of Ar–H with the nitronium cation NO_2^+, with the nitrosyl cation NO^+, and with the monomer of nitrogen dioxide NO_2, which also favors their formation.

The above considerations may also be applied to the understanding of the characteristics of certain other reactions.

EXPERIMENTAL

1. Nitration of benzene with dilute nitric acid in sealed tubes. Nitration was performed in two sealed tubes, capacity about 100 ml. In each of these was charged 20 ml benzene, 20 ml nitric acid, specific gravity 1.1, 10 g potassium nitrate and 0.2 g trioxymethylene (the latter to speed up formation of oxides of nitrogen). Heating at 135° was continued for 10 hours. The contents of the tubes were combined and treated first with water and then with soda solution. Acidification of the soda extract gave 0.52 g picric acid, m.p. 117-120° (no depression in mixed melting point test). Distillation of the organic layer by heating to 135° at the ordinary pressure brought over benzene. Distillation was then continued in vacuum (12 mm) when 0.62 g nitrobenzene came over. The residue (0.48 g) in the distillation flask crystallized and gave a positive reaction with dilute alkali for symm.-trinitrobenzene. After a single recrystallization from alcohol the product melted at 118° and did not depress the melting point of an authentic specimen of symm.-trinitrobenzene.

2. Nitration at normal pressure. 100 ml nitric acid (specific gravity 1.32), 1 l benzene and 2 g trioxymethylene were heated in a flask under a reflux condenser for 50 hours at a bath temperature of 60-65°. The acid layer was then separated and replaced by a fresh portion of nitric acid and trioxymethylene prior to continued heating for another 50 hours. The benzene layer was worked up as in the preceding experiment with water and soda solution. From the soda extract was obtained 1.6 g pure picric acid. The benzene was driven off from the organic layer under a low vacuum; then at about 80° and a pressure of 6 mm, nitrobenzene (12 g) came over. The residue of 2.41 g in the distillation flask was steam-distilled. The oily distillate (0.6 g) was not further examined; the residue (1.5 g)partly crystallized and gave a definite reaction for symm.-trinitrobenzene. Recrystallization from alcohol yielded 0.7 g trinitrobenzene with m.p. about 118° (no depression in the mixed melting point test).

3. Demonstration of formation of symm.-trinitrobenzene on nitration of benzene with nitric acid through the intermediate interaction of the hydrocarbon with nitrogen dioxide. a) For the heterogeneous reaction. Into each of two tubes was charged 2 ml benzene and 40 ml nitric acid (s.g. 1.1). To one of the tubes was added 8 g ammonium nitrate to destroy any nitrogen dioxide that might form. To the other tube was added 10 g potassium nitrate together with 0.05 g trioxymethylene for promoting nitrogen dioxide formation. Both of the tubes were heated for 4 hours at 120°. In the first tube, i.e. the one in which nitrogen dioxide could not be formed, the benzene was entirely unchanged and could be distilled off on the water bath. In the case of the second tube, using the previously described method, separation was effected of 0.07 g trinitrobenzene and 0.05 g picric acid.

Similar experiments using nitric acid of s.g. 1.2 gave (in absence of nitrogen dioxide) 0.12 g nitrobenzene and (in presence of nitrogen dioxide) 0.15 g trinitrobenzene, 0.1 g picric acid and about 0.1 g nitrobenzene. Experiments with nitric acid of s.g. 1.3 gave (in absence of nitrogen dioxide) 1.77 g nitrobenzene and (in presence of nitrogen dioxide) 1.7 g nitrobenzene, 0.15 g trinitrobenzene and 0.2 g picric acid.

b) For the homogeneous reaction. Into each of two tubes was charged 2 ml benzene, 15 ml glacial acetic acid and 5 ml nitric acid, s.g. 1.4. To the first tube was added 0.5 ammonium nitrate to destroy any nitrogen dioxide that might be formed, and to the second tube was added 0.1 g trioxymethylene to promote nitrogen dioxide formation. From the reaction mass of the first tube (i.e. in the absence of nitrogen dioxide) was obtained 1.02 g nitrobenzene and traces of nitrophenols. From the second tube, in which the reaction proceeded in presence of nitrogen dioxide, were separated 0.8 g nitrobenzene, 0.12 g crystalline symm.-trinitrobenzene and 0.17 g picric acid.

SUMMARY

In conformity with the previously developed theory it was found that the nitration of benzene with dilute nitric acid of s.g. below 1.2 proceeds substantially only through intermediate interaction with nitrogen dioxide and leads to the formation of a mixture of approximately equal parts of symm.-trinitrobenzene, picric acid and nitrobenzene. Increasing concentrations of nitric acid leads to an increase in the content of nitrobenzene, formed with participation of nitrogen dioxide, in the reaction product.

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THE BEHAVIOR OF KETONES TOWARDS AMMONIACAL SILVER OXIDE SOLUTION

V. I. Veksler

In the scientific literature and in textbooks is firmly entrenched the statement that an ammoniacal solution of silver oxide is a specific reagent for aldehydes which permits aldehydes to be differentiated from ketones (the silver mirror test [1]). In Liebig's handbook [2] it is stated that the reagent is prepared by adding to the aldehyde under test a small amount of ammonia and a solution of silver nitrate. Tollens [3] points out that the addition of excess ammonia sharply diminishes the sensitivity of the reagent described by Liebig. With the aim of eliminating this danger and also of increasing the sensitivity, he recommends the addition of caustic alkali to the reagent. Addition of alkali has also been recommended for the purpose of oxidizing aldehydes [4]. It must be pointed out that many authors have referred to the silver mirror reaction without being clear as to whether or not alkali is present.

In the literature we have only found one reference to an α,β-unsaturated ketone (3-methylcyclohexene-2-one-1) capable of giving the silver mirror reaction [5]. The reaction is also given by aliphatic diketones [6]. No indications of the ability of saturated monoketones to react with ammoniacal silver oxide solution have been found in the literature. However, as our investigations have shown, some ketones react with extraordinary ease with the ammoniacal silver oxide solution prepared by Tollens' method (with addition of caustic alkali). Examples are methylbenzyl ketone, dibenzyl ketone, p-tolylacetone, and unsymm. diphenylacetone. On addition of the reagent to the ketone in the cold, the solution at once darkens, black metallic silver is later precipitated, and a brilliant metallic mirror is formed on the walls of the vessel. The course of the reaction is particularly clear in the case of methylbenzyl ketone, p-tolylacetone and dibenzyl ketone. Unsymm. diphenylacetone reacts much more slowly. The reaction velocity is at a maximum during the first two hours, after which it rapidly slows down, coming practically to a standstill after 48-72 hours.

The data presented below for the behavior of ketones towards ammoniacal silver oxide solution were obtained predominantly with methylbenzyl ketone. We established that the reagent prepared from silver nitrate and ammonia in the absence of alkali does not act upon ketones in the cold (various ratios were tested, ranging from 2.3 to 10 moles NH_3 per mole $AgNO_3$). Addition of alkali in the equivalent amount (in relation to the silver) leads to an intense reaction. The excess of alkali acts as an accelerator. A large excess of ammonia hinders the reaction (see Table 1). Thus the inhibiting action of excess ammonia on the oxidation of aldehydes by silver oxide, as described in the literature [3], is also characteristic of the present reaction. The inhibiting effect is also reported in the literature in relation to oxidation of monohydric alcohols, oxycarbonyl compounds and oxyacids [7,8,11].

We also investigated the action of the reagent prepared by solution in ammonia of freshly precipitated and washed silver oxide. It was revealed that this reagent intensively oxidizes the ketones mentioned even without addition of caustic alkali. This may be explained by the obstinate retention by the precipitated silver oxide of part of the precipitating agent (alkali) [12]. The amount of silver oxide actually participating in the reaction (over a period of 48-72 hours) when using a solution with a given concentration of silver, alkali and ammonia was found to depend also on the relative amounts of starting substances: the higher the ratio of silver oxide to ketone the larger the amount entering into reaction. Thus, for the case investigated, when the initial ratio of Ag_2O to ketone was raised from 0.23 to 3.42, the consumption of silver oxide increased from 0.22 to 0.65 mole per mole of initial ketone (Table 2).

Examination of the products of reaction of ketones with the silver reagent did not reveal the presence of carboxylic acids which are the characteristic end products of conversion of aldehydes under similar conditions. Apart from metallic silver the reaction products contain resinous substances of a neutral character. Methylbenzyl ketone yielded a liquid resin with a yellow color which hardened slowly in the air, but rapidly in presence of acid. Similar products were obtained from the other ketones. Colloidal solutions containing an organic resin and metallic silver in the form of a stable sol were sometimes formed in experiments using a low concentration of alkali and also high dilutions.

At present it is impossible to explain the mechanism of the above reaction. The ability of ketones to react with ammoniacal silver oxide solution must be intimately bound up with the characteristic structures of ketones. The ketones investigated are characterized by the general structure $ArCH_2COR$ or Ar_2CHCOR, where Ar is an aromatic radical. All these ketones contain the $-CH_2-$ (or $>CH-$) group arranged between an aromatic group and carbonyl, and the carbonyl group is located in the β-position to the aromatic radical. Ketones lacking this characteristic structure are incapable of entering into reaction with ammoniacal silver oxide solution. We have thus found that the following do not react under the described conditions: Methyl hexyl ketone, which does not contain an aromatic radical; benzylacetone, in which the carbonyl group is separated from the phenyl radical by two CH_2 groups; propiophenone, in which the carbonyl group directly adjoins the aromatic nucleus. It is impossible to assert that the ability of ketones to enter into the reaction is associated with enolization, since ethylacetoacetate does not react with the silver reagent under the specified conditions.

Ketones of the general formula $ArCH_2COR$ or Ar_2CHCOR are distinguished by the presence of a reactive hydrogen in the CH_2 and CH groups, due to the influence of the carbonyl group and the aromatic radical. This feature actually distinguishes them from the series of investigated ketones incapable of reacting with the silver reagent, and evidently this characteristic determines the course of the reaction.

It may be suggested that silver oxide first oxidizes the CH_2 or CH group and that the resultant oxidation products then condense with formation of resins. It is possible, however, that condensation of the ketone takes place under the influence of the alkali in presence of the complex silver ions, and the resultant condensation products undergo oxidation (followed by condensation). Either of these mechanisms will be facilitated by the presence of an active CH_2 or CH group.

We carried out blank experiments to clarify the action of aqueous solutions of alkali and ammonia (in the absence of silver) on methylbenzyl ketone. It was found that on prolonged standing (several weeks) the ketone is converted into a liquid resin which gradually hardens in the air. The aqueous layer then gives the silver mirror reaction on addition of an ammoniacal silver oxide solution, although it no longer contains ketone. The absence of the latter is confirmed by the failure of the organic substance extracted from the aqueous layer to react with semicarbazide. These facts support the second mechanism which assumes that the first step is condensation, followed by oxidation. It must be admitted, however, that in experiments on the oxidation of the ketone with the silver reagent, the starting ketone was identified in the reaction mixture after the lapse of 24 hours in spite of the presence of unconsumed silver oxide. Consequently it is impossible to assert that the ketone at first entirely undergoes condensation, and therefore the results of the blank experiments cannot be regarded as evidence of the mechanism of the reaction.

EXPERIMENTAL

Investigated ketones. Methylbenzyl ketone, synthesized according to [9], b.p. 110-115° (25 mm), $n_\alpha^{20.5}$ 1.51168, $n_\beta^{24.5}$ 1.52857, semicarbazone m.p. 181-183°; p-tolylacetone synthesized according to [10], b.p. 117-118° (16 mm); dibenzyl ketone was purified via the semicarbazone, m.p. 33°; diphenylacetone, m.p. 61°; benzylacetone, prepared by hydrogenation of benzalacetone, b.p. 230-232°. In the control experiments freshly distilled ketones were used.

To a weighed amount of ketone in a flask of ordinary glass was added the oxidizing reagent, the flask was shaken several times by hand and then left to stand at room temperature. The progress of the reaction was followed by titration of samples with 0.01 N KCNS solution.

1) A silver oxide precipitate was obtained by the action of potassium hydroxide on silver acetate in the cold; it was filtered, washed with water, dissolved in ammonia (silver concentration $2.23 \cdot 10^{-5}$ g-equiv/ml; ammonia concentration $1.1 \cdot 10^{-6}$ mole/ml). To 1 g methylbenzyl ketone was added 300 ml of the ammoniacal solution. The solution became noticeably darker after a few minutes and a silver mirror was subsequently formed. The silver content of the solution after 24, 72, and 144 hours was respectively 0.46, 0.31, and $0.29 \cdot 10^{-5}$ g-equiv./ml (temperature 13-16°).

2) The oxidizing solution was prepared by adding sodium hydroxide and ammonia to a silver nitrate solution (silver concentration $2.25 \cdot 10^{-5}$; ammonia concentration $2 \cdot 10^{-4}$; concentration of excess alkali $2.3 \cdot 10^{-5}$ g equiv/ml). 250 ml of the solution was run into 1.5 g methylbenzyl ketone. After 24 hours the silver content of the solution was $0.35 \cdot 10^{-5}$ g-equiv/ml. The aqueous solution was run through a filter, the precipitate on the

filter and at the bottom of the flask (mirror) was washed with alcohol and then carefully washed several times with ether. After evaporation of the solvents in vacuum, the alcohol-ether extract gave 0.8 g of viscous resin with a light-yellow color. The resin gradually hardened when kept in a desiccator over calcium chloride. The aqueous layer was extracted with ether; evaporation of the ether left 0.3 g oil which formed a semicarbazone with m.p. 179-180°; the melting point of the mixture with the semicarbazone of the original ketone was 179-181°. The precipitate on the filter and at the bottom of the flask (metallic silver) dissolved completely in 50% HNO_3.

3) The oxidizing solution was prepared from equivalent amounts of $AgNO_3$ and NaOH with addition of ammonia until the Ag_2O precipitate dissolved. 200 ml of the solution was added to 0.5 g methylbenzyl ketone. After 72 hours the silver concentration had fallen from 3.3 to $0.8 \cdot 10^{-5}$ g-equiv/ml. The aqueous solution was poured through a filter, the precipitate on the filter and at the bottom of the flask was repeatedly treated with ether. The ether extract was evaporated in vacuum, leaving a viscous resin with a pleasant fresh odor.

With the aim of checking the ketone content of the resin, it was treated with alcohol when it partially dissolved. Semicarbazide solution was added to the alcoholic extract; a resin was precipitated which was completely soluble in ether; no semicarbazone was obtained.

After evaporating the ethereal solution of the resin in a vacuum desiccator over sulfuric acid, the residue had a yellow-orange color and could be readily ground to a powder. This had a faint odor. It softened and melted gradually over the range of 92-120°.

When the resin from which the ethereal extract had been made had been kept over sulfuric acid in a vacuum desiccator for several days, it was converted into a fine red powder with a faint odor, melting gradually between 62-75°.

0.0885 g substance: 0.2638 g CO_2. 0.0851 g substance: 0.2532 g CO_2; 0.0500 g H_2O. Found %: C 81.3, 81.2; H 6.6. $C_9H_{10}O$. Calculated %: C 80.6; H 7.05.

4) Mixtures were prepared from silver oxide and silver nitrate with various proportions of alkali and ammonia. To the mixtures were added weighed amounts of methylbenzyl ketone. After 72 hours samples were titrated. Some data illustrating the results obtained are presented in Table 1.

TABLE 1

CONSUMPTION OF SILVER OXIDE FOR OXIDATION OF METHYLBENZYL KETONE AS A FUNCTION OF THE INITIAL CONCENTRATION OF ALKALI AND AMMONIA (after 72 hours)

No.	Weight of ketone		Vol. of solution (ml)	Concentration of initial reagents (g-equiv/ml)				Consumption of silver (g-equiv · 10^5)	Molar ratio of consumed Ag_2O to initial ketone
				Silver ($\cdot 10^5$)		NaOH	NH_3 ($\cdot 10^4$)		
	g	mole · 10^4		Taken in form of Ag_2O	Taken in form of $AgNO_3$				
1	0.057	4.26	20	2.48	–	–	1.5	34.8	0.41
2	1.0	75	300	2.23	–	–	1.1	585	0.39
3	0.057	4.26	20	2.48	–	$5 \cdot 10^{-6}$	1.5	36.4	0.43
4	0.057	4.26	20	2.48	–	$5 \cdot 10^{-4}$	1.5	49.2	0.53
5	0.057	4.26	20	–	1.83	–	0.9	0	0
6	0.057	4.26	20	–	1.90	$4.5 \cdot 10^{-7}$	1.3	0	0
7	0.057	4.26	20	–	1.83	$5 \cdot 10^{-6}$	0.9	8.4	0.1
8	0.057	4.26	20	–	1.83	$5 \cdot 10^{-5}$	0.9	35.6	0.42
9	0.057	4.26	20	–	1.83	$5 \cdot 10^{-4}$	0.9	36.6	0.43
10	0.057	4.26	23	–	1.82	$4.4 \cdot 10^{-5}$	43.5	0	0

A sample of experiment 10 was placed in a vacuum desiccator in the cold under a residual pressure of 25 mm. With progressive loss of ammonia the reaction (darkening and a silver precipitation) became more and more intense.

5) Weighed amounts of methylbenzyl ketone were taken in the approximate ratios of 1:2:4:8:16.* To each was added 25 ml alkaline ammoniacal silver oxide solution (silver concentration $2.25 \cdot 10^{-5}$; ammonia concentration $2.0 \cdot 10^{-4}$; excess alkali as calculated $2.3 \cdot 10^{-5}$ g-equiv./ml). After 96 hours the silver concentration was determined and the consumption of Ag_2O per mole of ketone was calculated. Data showing the relation between silver oxide consumption and the initial ratio of reagents are presented in Table 2.

* Publisher's note. The ratios are actually those of Ag_2O to ketone (see third column of Table 2).

TABLE 2

DEPENDENCE OF THE CONSUMPTION OF SILVER OXIDE ON THE RATIO OF SILVER OXIDE TO KETONE

Weight of ketone		Initial molar ratio Ag_2O: ketone	Final silver concentration (g-equiv/ml · 10^5)	Molar ratio of Ag_2O consumed to initial ketone
g	mole			
0.1630	$1.2 \cdot 10^{-3}$	0.23	0.09	0.22
0.0975	$0.73 \cdot 10^{-3}$	0.38	0.67	0.27
0.0450	$0.43 \cdot 10^{-3}$	0.83	0.25	0.37
0.0220	$1.6 \cdot 10^{-4}$	1.71	1.48	0.58
0.0110	$0.82 \cdot 10^{-4}$	3.42	1.83	0.64

6) 0.05 g methylbenzyl ketone was allowed to stand with 140 ml of 2.5% solution of NaOH. After 18 days a liquid resin (0.25 g) with a yellow color had formed at the bottom. Part of filtrate (90 ml) was extracted several times with ethyl acetate. After driving off the solvent there remained 0.1 g of liquid which did not react with semicarbazide. To the remaining 50 ml of filtrate was added 10 ml of ammoniacal (alkaline) silver oxide solution (silver concentration $3 \cdot 10^{-6}$ g-equiv/ml). Darkening immediately developed. By the next morning there was no silver in solution, and at the bottom was a precipitate of metallic silver, also an organic substance. Consequently the aqueous layer contains a substance which does not react with semicarbazide but is susceptible to oxidation by ammoniacal silver oxide solution.

SUMMARY

It is shown that a series of alkaryl ketones of the general formula $ArCH_2COCH_3$ or $Ar_2CHCOCH_3$ reacts in the cold with alkaline ammoniacal silver oxide solution to form a silver mirror. In the light of these data the alkaline ammoniacal silver oxide solution is not a specific reagent for differentiating aldehydes from ketones.

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THE ACTION OF ETHYL CHLOROCARBONATE UPON ORGANOMAGNESIUM COMPOUNDS

A. I. Krutman

The reaction between organometallic compounds and esters of haloacids was first studied by A. M. Butlerov [1]. He obtained the following reaction on treating methyl zinc with ethyl chlorocarbonate: $2ClCOOC_2H_5 + Zn(CH_3)_2 = 2CO_2 + 2C_2H_4 + 2CH_4 + ZnCl_2$. On reacting methyl zinc with methyl chlorocarbonate Butlerov obtained: CO_2, CH_3Cl and C_2H_4. In 1903 a paper appeared by A.N. Reformatsky [2] on the synthesis of tertiary alcohols by the action of allyl iodide and zinc on esters of halo acids in ethereal solution, when he obtained alcohols with three olefinic bonds. He proposed a reaction mechanism. Later authors [3] worked with esters of halo-substituted acids and halogenated organomagnesium compounds. Later still Iotsich [4] obtained triallylene carbinol and Matsurevich [5] triethyl carbinol and tripropyl carbinol.

The aim of our investigation was the further study of this reaction and the preparation with its help of substances about which little has been published. Our researches indicate the applicability of this reaction not only to the preparation of tertiary alcohols but also to the preparation of esters. For the preparation of the former a large excess of the organomagnesium compound is taken and is added to the chlorcarbonic ester, while for the preparation of esters the starting products are taken in equal amounts, the chlorocarbonic ester being added to the formed organomagnesium compound. The reaction proceeds according to the scheme put forward by A.N. Reformatsky. It can likewise proceed according to Houben's scheme.

EXPERIMENTAL

1. Synthesis of triallylcarbinol. Allyl magnesium bromide was prepared in a three-necked round-bottomed flask fitted with a mercury seal, a mechanical stirrer, a reflux condenser and a dropping funnel. Its yield was checked by titration of a sample with 0.1 N sulfuric acid using methyl orange as indicator. Through one of the necks of the flask was inserted a siphon, and a second opening served for withdrawal of samples. During the reaction the latter opening was closed. For the performance of the second stage of the reaction, i.e. the reaction with ethyl chlorocarbonate, the ethereal solution of allyl magnesium bromide was siphoned under pressure of dry hydrogen into another flask likewise equipped with mechanical stirrer, reflux condenser and dropping funnel. A special device was inserted in the siphon for trapping the fine magnesium turnings. In the course of stirring over a period of two hours addition was made to the ether solution of the complex of the calculated amount of freshly distilled ethyl chlorocarbonate dissolved in three times the volume of absolute ether. With progressive addition of the ethyl chlorocarbonate the temperature of the liquid rose and it became lighter in color. The reaction was completed by heating on a hot water bath. The end of the reaction was checked by the color reaction of Gilman and Schultze [6]. The contents of the flask were then decomposed with ice and sulfuric acid, and the ether layer was separated from the aqueous layer. The latter was twice extracted with ether and the extracts added to the main layer. The combined ether layer was washed with 10% sodium carbonate solution and after separation it was dried with calcium chloride. The ether was distilled off, leaving in the flask a yellowish liquid boiling at 189-192°. This was a mobile liquid with a faint yellow color and a terpene-like odor, insoluble in water, readily soluble in alcohol and ether. It does not oxidize in the air. After keeping for about a year the preparation had scarcely changed in boiling point. Its constants and analysis are detailed in Table 1. It gave a positive reaction for tertiary alcohols in the Deniges test [7]. The phenylurethane melts at 239°. All the analyses confirm the preparation of triallylcarbinol.

This carbinol was prepared for the first time by A.N. Reformatsky [8] by the action of zinc on 1 mole ethyl chlorocarbonate and 3 moles allyl iodide in ether solution. The experiment lasted 3 months. Reformatsky attempted to conduct the reaction in presence of metallic magnesium (in place of zinc), but it proceeded rather stormily with much heat development even with good cooling and slow addition of the ethereal solution of the mixture of allyl

TABLE 1

Triallyl carbinol	B. p.	d_4^{21}	n_D^{21}	MR_D	Parachor*	Found % C	Found % H	Reaction with C_6H_5NCO	% OH*	Duration of expt.	Yield (in %)
Our preparation	189-192°	0.8791	1.468	47.8933	391.2	78.41 79.31	10.62 10.82	Reacts	10.88	10-12 hours	66.66
Reformatsky's preparation [8]	191-192°	0.8781	1.468	47.8933	–	78.64 78.52	10.76 10.63	–	–	3 mos.	27.50

* $C_{10}H_{16}O$. Calculated: MR_D 48.15; P 404.5; %: C 78.94, H 10.52; OH 10.17.

TABLE 2

Tri-n-butylcarbinol	B. p.	d_4^{15}	n_D^{15}	MR_D*	Parachor*	Found % C	Found % H	Reaction with C_6H_5NCO	% OH*	Yield (in %)
Our preparation	129-132° at 20 mm	0.8332	1.4370	62.338	550.4	77.65 77.94	13.74 14.38	Reacts	8.2	81.25
Ivanov's preparation [10]	120 at 10 mm	d_4^{15} 0.8440	n_D^{15} 1.4448	–	–	–	–	Does not react	–	51.00

* $C_{13}H_{28}O$. Calculated MR_D 63.76; P 554.59; %: C 78.00; H 14.00; OH 8.5.

iodide and haloester to the magnesium. This variant was therefore considered unsuitable for the preparation of unsaturated compounds. Reformatsky's method also involved large losses of allyl iodide by evaporation over the long period of the reaction.

2. Synthesis of tri-n-butyl carbinol. Butyl magnesium bromide prepared in the above-described apparatus by the usual method was transferred to the other flask. Ethyl chlorocarbonate was introduced over a period of 2 hours. Heat was evolved also in this reaction. The reactionproduct was decomposed and worked up as in Experiment 1. Following the distillation of the ether the flask contained a syrupy, light-yellow liquid. Fractionation yielded a fraction boiling at 129-132° (20 mm). Its constants and analysis are detailed in Table 2. The phenylurethane formed light-yellow crystals, m.p. 147.5°. Deniges' reagent gave a negative result.

Tri-n-butylcarbinol was obtained by Moyer and Marvel [9] from butyl magnesium bromide and ethyl carbonate in 84% yield. B. p. 129-131° (20 mm). Some data are reported by Ivanov [10] who obtained the alcohol from butyl magnesium bromide and CO_2.

3. Synthesis of triisoamylcarbinol. Isoamyl magnesium bromide was prepared by the usual method. The procedure for the second stage of the synthesis was the same as above. After removal of the ether the flask contained a colorless, viscous liquid which was distilled under reduced pressure. Fractionation yielded a fraction with b. p. 136-140° (at 10 mm), soluble in alcohol and ether. Yield 88% of the theoretical. Negative reaction in the Deniges test. d_4^{20} 0.8362; n_D^{20} 1.443; MR_D 75.088; calculated 77.61; σ 30.61.

Parachor. Found: P 680.6; calculated 671.5. Found %: C 79.39; H 14.10; OH 6.63. $C_{16}H_{34}O$. Calculated %: C 79.30; H 14.05; OH 7.02. The phenylurethane melted at 147.8°.

Triisoamylcarbinol was first prepared by Grignard [11] from carbonyl chloride and isoamyl magnesium bromide with b. p. 140° (10 mm). There are no other data in the literature.

4. Synthesis of ethyl propionate. The prepared ethyl magnesium bromide was charged into a flask containing the equivalent amount of ethyl chlorocarbonate. Fractionation of the reaction product gave a fraction (yield 50%) boiling at 99-105°; d_4^{18} 0.9547; n_D^{20} 1.333; MR_D 26.709; calculated 26.944. Analysis of the silver salt of propionic acid following hydrolysis of the ester: Ag 61.02%; Calculated 59.64%. Only the following constants appear in the literature [12] for ethyl propionate: b. p. 98-99°; d_4^{20} 0.8907.

5. Synthesis of ethyl valerate. The method of preparation was the same as in the preceding experiment.

Fractionation gave a fraction (yield 26%) boiling at 32-40° (10 mm); d_4^{20} 0.8828; n_D^{20} 1.412; MR_D 36.18. The prepared ester was hydrolyzed. The silver salt of valeric acid gave (%): Ag 50.29; calculated: 51.64. In the literature the following constants are reported for ethyl valerate [13]: b.p. 144.4° (at 736.5 mm); d^{20} 0.8765.

6. Synthesis of ethyl isocaproate. Preparation was by the same method as in the previous experiment. Yield 28% of the theoretical. A fraction boiling at 50-53° (10 mm) was isolated; d_4^{20} 0.8700; n_D^{20} 1.405; MR_D 39.72; calculated 40.11. The ester was hydrolyzed and the silver salt of isocaproic acid was obtained. Found (%): Ag 47.97; calculated 48.38. The constants given in the literature [14] for ethyl isocaproate are: b.p. 160.4° (737 mm); d^{20} 0.8705.

SUMMARY

1. In a series of experiments it was established that tertiary alcohols (both saturated and unsaturated) and esters are obtained by the reaction of ethyl chloro-carbonate with organomagnesium compounds.

2. Tri-n-butylcarbinol and triisoamylcarbinol (about which there is little information in the literature) were prepared and investigated.

3. The method of preparation of triallylcarbinol has certain advantages over Reformatsky's method, namely: Reduction in the duration of the reaction from 3 months to 10-12 hours and a considerable decrease in the loss of starting materials.

4. The Deniges reaction is not characteristic for all tertiary alcohols. In particular it gives negative results with tri-n-butylcarbinol and triisoamycarbinol.

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BIS-TRICHLOROPHOSPHAZOSULFONE

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For the purpose of investigating the trichlorophosphazosulfone grouping (I) it would be interesting to have a compound in which the properties of the trichlorophosphazosulfone group were not obscured by those of any other combined groups.

At the present time two types of phosphazosulfone compounds are known: Trichlorophosphazosulfone aryls (II) [1] and the anhydride of trichlorophosphazosulfuric acid chloride (III) [2]. In the first type the trichlorophosphazosulfone group is combined with various aryl radicals, in the secondtype with chlorine. Consequently in the trichlorophosphazosulfone aryls the properties of the aryl radicals are superposed on those of the trichlorophosphazo group, and the anhydride of trichlorphosphazosulfuric acid is both a trichlorophosphazosulfone compound and the anhydride of a chlorosulfonic acid.

A compound with a "pure" trichlorophosphazosulfone group not bound to any "foreign" groups is bistrichlorophosphazosulfone (IV) which is undoubtedly the best model for a study of the properties of the trichlorophosphazosulfone group. Compound (IV) has so far be en unknown. The objective of the present investigation was its preparation.

$-SO_2-N{=}PCl_3$ (I); $ArSO_2N{=}PCl_3$ (II); $ClSO_2N{=}PCl_3$ (III); $Cl_3P{=}NSO_2N{=}PCl_3$ (IV).

For the purpose of preparation of bistrichlorophosphazosulfone the same route was selected as for the preparation of other trichlorophosphazosulfone compounds [1,2], i.e., the action of phosphorus pentachloride on the appropriate sulfamide, in this case the simplest sulfamide, according to the equation:

$$2PCl_5 + NH_2SO_2NH_2 \rightarrow 4HCl + Cl_3P{=}NSO_2N{=}PCl_3.$$

It transpired that the reaction proceeds very readily in this direction, even at room temperature, and is accompanied by development of heat. At 100° the reaction proceeds violently and is completed in a few minutes. It is more convenient to perform the reaction at first at 50-60° and to raise the temperature to 100° only towards the end. If the selected reactants are chemically pure substances in exactly stoichiometric proportions, or, better, with a slight excess of phosphorous pentachloride, then the quantity of hydrogen chloride separated and the amount of bistrichlorophosphazosulfone formed are respectively within 1.0 and 0.3% of the theoretical amounts.

As first prepared, bistrichlorophosphazosulfone is a colorless liquid resembling glycerol in viscosity and appearance. After two weeks one of the specimens had crystallized to a lustrous, perfectly dry and very hard mass melting at 40.5 (maximum from 39°) - 41.5° (the latter with the thermometer bulb immersed in the liquid). The melted substance very easily supercools, and in the absence of seeds it can be kept in liquid form at room temperature for many days. The substance is readily soluble in benzene, toluene, ether and acetone; difficultly soluble in petroleum ether. Bistrichlorophosphazosulfone does not fume in the air but very quickly deliquesces. Fine crystals of the compound react quietly with water. When larger crystals (0.2-0.3g) are introduced into water, the substance at first spreads out and then rapidly dissolves with evolution of heat and with a characteristic noise. Large amounts react with water instantaneously and very violently. If a small quantity of bistrichlorophosphazosulfone is placed on a wet filter paper, a violent reaction starts within a few seconds, the paper chars, and a strong odor of burnt sugar is developed. Bistrichlorophosphazosulfone vigorously reacts with aqueous and anhydrous ammonia, amines, alcohols, phenols, and organometallic compounds. In a vacuum of 0.5 mm it does not distill undecomposed.

Bistrichlorophosphazosulfone is very difficult to recrystallize because of its exceptional ease of solution in the majority of organic solvents; from a mixture of solvents with petroleum ether it separates as an oily layer.

About 50 g of substance separates from a solution of 110.0 g bistrichlorophosphazosulfone in 5.0 ml benzene at 20°. Consequently, at 20° about 60 g bistrichlorophosphazosulfone is dissolved in 5.0 ml benzene. The bistrichlorophosphazosulfone obtained by recrystallization from benzene is in the form of large, colorless, transparent platelets with a length of up to 8 mm. It will be well understood that all possible precautions against access of moisture from the air must be applied to the substance and its solution. Fortunately, the preparation of chemically pure bistrichlorophosphazosulfone does not necessitate recrystallization, for the perfectly pure substance can be

easily obtained directly from the reaction without any special purification, but this calls for the use of perfectly pure starting materials and thorough removal of the excess of phosphorus pentachloride by heating in vacuum.

EXPERIMENTAL

Quantitative experiment. Into a round-bottomed two-necked 100 ml flask were introduced 0.21 mole pure phosphorus pentachloride (43.74 g) and 0.1 mole pure sulfamide (9.61 g) which had been thoroughly dried in vacuum. A cork was at once attached in which was inserted a reflux condenser with a broad tube serving as a receiver for the excess phosphorus pentachloride, and a narrow tube for escape of the hydrogen chloride. A slow stream of dry air was passed through the second tube throughout the whole period of the experiment. The top end of the reflux condenser was connected to two absorbers containing 0.6 equivalents of potassium hydroxide dissolved in 900 g water. The flask was rotated and shaken to facilitate mixing of the sulfamide with the phosphorus pentachloride. Hydrogen chloride at once begins to come off, as indicated by the "currents" in the first absorber. Through the reflux condenser is passed iced water in order to retain the phosphorus pentachloride as well as possible, and the flask is immersed in a water bath heated to 60°. Evolution of hydrogen chloride is intensified; after a few minutes the reaction mixture begins to liquefy and after 6-7 minutes it has the appearance of a semiliquid gruel. After 20 minutes the bath temperature is raised to 90° and after 30 minutes the reaction is at an end. The reaction mass is a colorless, transparent liquid in which float a few particles of excess phosphorus pentachloride. In the reflux condenser and on the cold parts of the flask is deposited a thin layer of phosphorus pentachloride. The stream of dry air is passed through for a further 15 minutes, after which the contents of the absorbers are mixed and made up with water to a weight of 1000 g.

Neutralization of 25.00 g of the solution required 24.52 ml 0.2 N acid. Found: 0.4038 equivalent of hydrogen chloride. Calculated (from the reaction equation): 0.4000 equivalent.

The amount of hydrogen chloride found is thus 0.95% more than the calculated amount. The probable explanation of this is that the phosphorus pentachloride was not fully condensed in the condenser tube and was partly entrained by the stream of hydrogen chloride and dry air. In order to remove the excess of phosphorus pentachloride, the tube through which air was blown was closed, the upper end of the condenser was connected to a vacuum and the flask was heated on a boiling water bath so that the entire surface of the flask was heated by steam. If this is not done, part of the phosphorus pentachloride is deposited in the neck of the flask. The phosphorus pentachloride is completely removed in the course of one hour at a vacuum of 6-8 mm and at the temperature of the boiling water bath. Bistrichlorophosphazosulfone remains in the flask in the form of a transparent, colorless liquid which at once crystallizes after cooling and seeding. Weight of product 36.81 g or 100.3% of the theoretical amount calculated on the sulfamide. M.p. 39.7-41.0. After heating in a 2 mm vacuum at 130° for 15 minutes, the melting point rose to 40.5-41.5°. Addition of a little dry benzene to the melted substance followed by cooling caused the bistrichlorophosphazosulfone to crystallize in the form of large, dense transparent platelets with the same melting point (see general part).

Preparation of bistrichlorophosphazosulfone. Into a round-bottomed half-liter flask are introduced 0.3 mole dry sulfamide (28.83 g) and 0.63 mole pure phosphorus pentachloride (131.24 g). The flask is closed with a cork through which passes a broad reflux condenser whose upper end is connected to a downwardly sloping glass tube 20-30 cm in length and 3-4 mm in diameter. This tube takes the place of a calcium chloride tube. The reaction mixture is well stirred by rotating the flask which is then placed on a water bath heated to 60-70°. The reaction proceeds as in the quantitative experiment. At the end of the reaction the upper end of the reflux condenser is connected to a vacuum and the total surface of the flask is heated, first for one hour on the boiling water bath and then for 15-30 minutes on an oil bath at 130°. Starting from perfectly pure substances, the yield of bistrichlorophosphazosulfone is about 100% of theory and the m. p. is 40.5-41.5°. If technical phosphorus pentachloride has been used the melting point is depressed by several degrees. Care should be taken that there is a slight excess of phosphorus pentachloride. When working with technical phosphorus pentachloride it must be remembered that it contains a fairly large proportion of phosphorus oxychloride so that it might easily happen that there is an excess of sulfamide. If there is a slight excess of sulfamide the melting point of the product is lowered by 3-4° and a large proportion of the sulfamide rapidly crystallizes from the liquid bistrichlorophosphazosulfone in the form of transparent thin platelets. For complete removal of the sulfamide the product must be dissolved in three times the volume of dry benzene, the sulfamide sucked off, and the benzene driven off in vacuum; however, it is best so to conduct the reaction that an excess of phosphorus pentachloride is present. For the properties of bistrichlorophosphazosulfone see the general part.

Analyses of bistrichlorophosphazosulfone. Analyses were performed on the substance with m. p. 40.5-41.5°, prepared from chemically pure materials. The molecular weight was determined by the cryoscopic method in benzene solution. Nitrogen, sulfur, phosphorus and chlorine were determined by the usual methods after hydrolysis of the weighed sample of bistrichlorophosphazosulfone in aqueous solution. The acids were titrated after hydrolysis, using thymolphthalein as indicator.

0.2114 g, 0.2367 g substance: 0.3723 g, 0.4162 g AgCl. 0.4979 g, 0.4857 g substance; 0.3158 g, 0.3095 g $BaSO_4$. 0.5891 g, 0.5426 g substance: 0.3560 g, 0.3274 g $Mg_2P_2O_7$. 0.7068 g, 0.7886 g substance: 19.35 ml, 21.62 ml 0.2 N. Acid. 0.1184 g, 0.1079 g substance: 19.41 ml, 17.68 ml 0.2 N alkali. 0.1591 g, 0.3291 g substance; 20.0 g benzene: Δt 0.112°, 0.235°. Found %: Cl 57.88, 57.80; S 8.71, 8.75; P 16.82, 16.79; N 7.67, 7.68. Equivalents of acid on hydrolysis: 12.03, 12.02; M 360.1, 355.0. $Cl_6SP_3N_3O_2$. Calculated %: Cl 57.99; S 8.74; P 16.89; N 7.68. Equivalents of acid on hydrolysis: 12.00; M 366.8.

SUMMARY

Bistrichlorophosphazosulfone has been prepared and some of its properties described.

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REACTIONS OF ALIPHATIC DIAZO COMPOUNDS WITH UNSATURATED COMPOUNDS

XI. THE REACTION OF ETHYL DIAZOACETATE WITH ALLYL CHLORIDE

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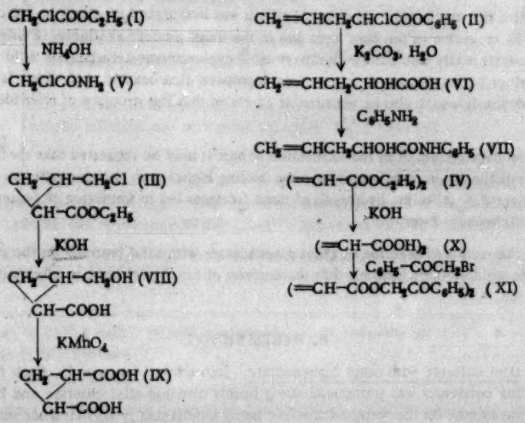
In one of the previous communications [1] of this series it was shown that reaction of ethyl diazoacetate with allyl bromide gives a 70% yield of the ethyl ester of α-bromallylacetic acid. The purpose of the present study is the examination of the reaction of ethyl diazoacetate with allyl chloride. The investigation has shown that in analogy with the allyl bromide reaction, the ethyl ester of α-chlorallylacetic acid is formed (II), but this is not the sole reaction product. By careful fractionation of the crude condensation product it was possible to isolate, in addition to the ester (II), the esters (I) and (III), while evidence was obtained of the presence of an ester (IV) in the fractions boiling higher than ester (III) (see experimental part).



The above reaction scheme also illustrates the further course of the investigation which was undertaken with the aim of establishing the structure of the compounds obtained. Compounds (II), (III), and (VII) are here described for the first time. Compounds (VI), (VIII) and (X) were not isolated in the analytically pure form in the course of this investigation. The first substance which we succeeded in isolating by fractionation of the crude reaction product was ethyl chloroacetate (I). This was identified by conversion into chloracetamide (V). The formation of ethyl chloroacetate during the reaction of ethyl diazoacetate with allyl chloride confirms the observations of Buchner [2] concerning the ability of ethyl diazoacetate to remove hydrogen halide from esters of halo-substituted acids. * It may be assumed that in our case the cleavage of hydrogen halide proceeded from ester (II) and not from ester (III) since the latter route is hardly probable [13]. However, the possibility is not excluded of direct cleavage of hydrogen halide from the allyl chloride which is present in the reaction mixture in large excess. No experimental confirmation of this possibility has yet been found.

* A fresh examination of the product of reaction of ethyl diazoacetate with allyl bromide showed that, in addition to the ester of α-bromallylacetic acid, a small amount of ethyl bromoacetate is also formed (see experimental part).

The second substance isolated during fractionation of the crude product was the ethyl ester of α-chlorallylacetic acid (II). It was hydrolyzed with potassium carbonate solution to give α-hydroxylallylacetic acid which we were unable to isolate in the perfectly pure form due to the small amount obtained. The acid was characterized by conversion to the anilide (VII) whose identity was confirmed by a melting point test in admixture with an authentic specimen and by determination of the nitrogen content.

The data obtained permit us to ascribe the formula (II) to the investigated chloride. Concerning the mechanism of formation of this chloride we may put forward the same two suggestions that were advanced when discussing the mechanism of formation of the ethyl ester of α-bromallylacetic acid [1].

In view of the fact that among the products of reaction of ethyl diazoacetate with allyl chloride was found the ester of 2-chloromethylcyclopropane-1-carboxylic acid(III) (see below), we took the opportunity of examining its susceptibility to isomerization into the unsaturated chloride (II) under conditions similar to those of its formation. The control experiment performed for this purpose gave a negative result: Prolonged heating of the investigated chloride with excess of allyl chloride in presence of cuprous chloride as catalyst did not reveal any influence on the starting chloride. The indicates that the cyclic chloride (III) cannot be an intermediate product in the synthesis of the unsaturated chloride (II) in the reaction here investigated.

The cyclic chloride (III) was the third substance isolated during fractionation of the crude reaction product. The chloride contained a trace of ethyl fumarate which we were able to eliminate by treatment with cold permanganate solution.

In order to establish the structure of the chloride (III) it was hydrolyzed by alkali to the cyclic hydroxy acid (VIII) which could not be separated in the pure form due to the small amount available. Evidence that the acid resulting from the hydrolysis really was trans-2-(hydroxymethyl)-cyclopropane-1-carboxylic acid was obtained by oxidizing it with potassium permanganate to trans-1,2-cyclopropane dicarboxylic acid which is well known in the literature. On this evidence it would also be permissible to claim that the structure of chloride (III) has been elucidated.

On the basis of the data presented in the experimental part it may be suggested that the fractions obtained by further fractionation of the crude reaction product and boiling higher than chloride (III) are a mixture of this chloride with ethyl fumarate.* Alkaline hydrolysis of these fractions led to formation of fumaric acid, characterized in the form of its diphenacyl ester.

Consideration of the results of reaction of ethyl diazoacetate with allyl bromide on the one hand, and of those with allyl chloride on the other, indicate that the activity of the C—Hal bond in allyl bromide is greater than that in allyl chloride. **

EXPERIMENTAL

Condensation of allyl chloride with ethyl diazoacetate. Into a round-bottomed flask fitted with a stirrer, dropping funnel and reflux condenser was introduced 600 g freshly distilled allyl chloride and 2.4 g cuprous chloride.*** The mixture was heated on the water bath while being mechanically stirred; after reaching the boiling point, slow addition was made from the dropping funnel (without stopping the heating) of 188.8 g ethyl diazoacetate mixed with an equal volume of allyl chloride. The evolved gas passed through a trap immersed in a freezing mixture and was collected in a gasholder. The total volume of evolved nitrogen was 33.52 l (15° and 767 mm) or 85% of theory.

The experiments showed that during the reaction the catalyst (cuprous chloride) underwent a partial change (color change to bright orange) and part went into solution to form a complex compound with allyl chloride.

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* In view of the fact that the boiling point of the investigated fractions is considerably above the boiling point of ethyl fumarate, it is possible that they are admixed with the product of the condensation of ethyl diazoacetate with the ester of the α-chlorallylacetic acid.

** Comparative evaluation of the relative activity of the halogen in allyl chloride, bromide and iodide was made by Tronov and Gershevich [3] who found that the activity ratio was 1:860:4300 (in reaction with pyridine) and 1:85:138 (in reaction with sodium methylate).

*** The condensation reaction was performed in presence of the following catalysts: Copper bronze (Natur cupfer C.) and cuprous chloride. It was found that the reaction does not proceed in presence of copper sulfate; with the other two catalysts equally good results are obtained (compare [1]).

These compounds were removed at the start of the reaction by filtering off the reaction mixture from the catalyst, washing with dilute hydrochloric acid (1:1) and then washing with sodium carbonate solution. In order to avoid loss of substance during these washing treatments, the wash liquors were extracted with ether, and the residues from the ether extracts (after removal of solvent) were added to the main bulk. The reaction mixture was then dried with calcium chloride and freed from excess allyl chloride by heating on the water bath. The remaining material, a dark-colored liquid, was distilled in a 10 mm vacuum without separation into fractions. In the distillation flask remained a large amount of thick, dark-colored resin. The distillate came over in a wide temperature range (from 40 to 110°) at 10 mm.

The resultant complex mixture of products was subjected to fractionation in a vacuum column with a dephlegmator at 10 mm. Even after repeated fractionation it was impossible to separate the constituents completely, but three main components were isolated, incidentally, in almost analytical purity (see introduction). The results of fractionation are shown in the table.

RESULTS OF FRACTIONATION OF CONDENSATION PRODUCTS

No. of fraction	B. pt.	Weight (in g)	Name of substance in fraction
1	40-41°	16.7	Ethyl chloroacetate
2	42-66	9.0	Intermediate fraction
3	66-67	16	Ethyl ester of α-chlorallylacetic acid
4	67-83	16.1	Intermediate fraction
5	83-87	11.9	Ethyl ester of 2-(chloromethyl)-cyclopropane-1-carboxylic acid
6	87-92	14.8	Ethyl fumarate in admixture with the cyclic chloride and with other chlorides
7	92-96	8.0	
8	96-100	6.0	
9	100-110	12.6	

Ethyl chloroacetate. (I). This was isolated in the analytically pure form by direct fractionation in a vacuum column (Table 1). B. pt. 40-41° (10 mm); 142-143° (760 mm); d_4^{20} 1.1406; n_D^{20} 1.4202; MR_D 27.20; calculated 27.19.

Found %: Cl 28.77, 28.81. M 123.3, 119.9. $C_4H_7O_2Cl$. Calculated %: Cl 28.96. M 122.56.

Literature data: B. pt. 142.6-143° at 750 mm [4]; 52° at 20 mm [5]; d_4^{20} 1.1520; n_D^{20} 1.4216 [4].

Chloroacetamide (V). 2 ml of the substance under investigation was shaken in a test tube with 2 volumes of 20% ammonia at 0°. The crystals of chloracetamide obtained after recrystallization from alcohol melted at 119-120° (no melting point depression in admixture with an authentic specimen).

Ethyl ester of α-chlorallylacetic acid (II). Like the chloride (I) it was separated in analytical purity by direct fractionation of the crude reaction product. B. pt. 66-67° (10 mm); d_4^{20} 1.0530; n_D^{20} 1.4400; MR_D 40.72; calculated 40.58.

0.1673 g substance: 0.1472 g AgCl. 0.2458 g substance; 17.1 g benzene: Δt 0.46°. 0.4171 g substance: 17.1 g benzene: Δt 0.78°. Found %: Cl 21.77; M 160.0, 160.4. $C_7H_{11}O_2Cl$. Calculated %: Cl 21.86; M 162.62.

Hydrolysis of the ester (II). Into a round-bottomed flask fitted with a stirrer and a mercury seal was introduced 14 g of the substance under examination and 119 g 10% potassium carbonate solution. Boiling and mechanical stirring of the reaction mixture were continued up to disappearance of the layer of oily ester (about 2 hours). The cooled solution was acidified with sulfuric acid (Congo red indicator) and extracted with ether. After drying the ether extract and distilling off the ether, there remained 3.3 g of viscous, dark-colored oil which we assumed to be α-hydroxyallylacetic acid.* The liquid did not, however, crystallize either on standing in a vacuum desiccator over sulfuric acid or on cooling to −10°. For the purpose of identification the acid was converted into the anilide by the method of Shriner and Fuson [6]. The crystals of anilide had a yellow color and were decolorized by boiling with animal charcoal. After recrystallization from alcohol the m. pt. was 77-78°.

0.1244 g substance: 7.8 ml N_2 (20°, 775.2 mm) 0.2042 g substance: 13.2 ml N_2 (19°, 772.7 mm). Found %: N 7.38, 7.61. $C_{11}H_{15}O_2N$. Calculated %: N 7.33

By a similar method we obtained the anilide of authentic α-hydroxyallylacetic acid. A mixture of both of the anilides did not exhibit any melting point depression.

Ethyl ester of 2-(chloromethyl)-cyclopropane-1-carboxylic acid (III). Fraction 5, Table 1 (crude chloride).

* We were the first to prepare this acid by hydrolysis of the ethyl ester of α-bromallylacetic acid. It formed very hygroscopic crystals melting at 37° [1].

B. pt. 83-87° (10 mm); n_D^{20} 1.4530.

0.1686 g substance: 0.1402 g AgCl. 0.2363 g substance: 0.1951 g AgCl. Found %: Cl 20.56, 20.42. $C_7H_{11}O_2Cl$. Calculated %: Cl 21.82.

In order to remove the admixed ethyl fumarate, 30.4 g of the crude chloride (III) was shaken in the cold with potassium permanganate until the violet color of the permanganate ion had disappeared; this required 17.0 g permanganate. After filtration, the manganese dioxide was washed with ether and the filtrate in turn was extracted with ether. The ether extracts were combined and dried, the ether distilled off, and the flask residue fractionated to give 21.1 g of a chloride with the following constants:

B. pt. 82-84° (8 mm); d_4^{20} 1.1091; n_D^{20} 1.4560; MR_D 39.87; calculated 38.87. Found: Increment for a three-membered ring 1.0.

0.1284 g substance: 0.1120 g AgCl. 0.2538 g substance: 0.2248 g AgCl. 0.1948 g substance; 17.32 g benzene: Δt 0.37°, 0.2673 g substance; 17.03 g benzene: Δt 0.52°. Found %: Cl 21.58, 21.89; M 156.0, 154.9. $C_7H_{11}O_2Cl$. Calculated %: Cl 21.86; M 162.62.

Hydrolysis of chloride (III). Into a flask with a reflux condenser were introduced 14.8 g cyclic chloride and 11.6 g potassium hydroxide dissolved in methyl alcohol. The reaction mixture was heated on the water bath for one hour. The precipitate of potassium chloride was filtered off, the excess alkali neutralized with carbon dioxide, the methyl alcohol removed by boiling with water on the water bath, and the residue after acidification was extracted with ether.

Removal of the ether left 8.1 g of syrupy liquid which we took to be 2-(hydroxymethyl)-cyclopropane-1-carboxylic acid (VIII). Part of the acid was used for preparation of the silver salt:

Found %: Ag 46.2. $C_5H_8O_3$. $C_5H_7O_3Ag$. Calculated %: Ag 48.54.

The low content of silver found in the silver salt indicates that the acid was impure.

Oxidation of the hydroxy acid (VIII). Oxidation of 3.9 g of acid (VIII) was effected by shaking its aqueous solution with an excess (2 g) over the calculated (7 g) amount of potassium permanganate. This required, in all, two days. The excess permanganate was destroyed with a few drops of bisulfate, the manganese dioxide filtered off, the solution was concentrated on the water bath, acidified with sulfuric acid and extracted with ether. From the ether extract was isolated 1.26 g (28.97% of theory) of a colorless, crystalline acid with a m.pt. 165°. After two crystallizations from water the m. pt. was constant at 172°.

Found %: C 46.51; H 5.04; equiv. 65.40. $C_5H_6O_4$. Calculated %: C 46.17; H 4.65; equiv. 65.05.

No melting point depression occurred when mixed with an authentic specimen of trans-cyclopropane-1,2-dicarboxylic acid prepared by one of us by another route [7].*

Investigation of the isomerizing tendency of the cyclic chloride (III). 8.9 g of chloride (III), 70 g allyl chloride and 0.2 g cuprous chloride were heated to boiling on the water bath with mechanical stirring for three hours. The catalyst was filtered off from the cooled solution and the filtrate well washed, first with dilute hydrochloric acid and then with soda solution as detailed above. The solution was then dried with calcium chloride, the excess allyl chloride was distilled off, and the residue distilled in vacuum. The constants of the distillate did not differ from those of the original chloride (III), so that we may conclude that chloride (III) is not susceptible to isomerization under the conditions of the investigated reaction.

Ethyl fumarate (IV). The percentage content of halogen was determined in fractions 7, 8 and 9 (see table) as, respectively, 15.30, 7.37 and 5.90. All three fractions were unsaturated in the permanganate test. Fraction 7 (7.7 g) was heated on the water bath for 30 minutes with a solution of 7.8 g potassium hydroxide in methyl alcohol. The precipitate of potassium chloride was filtered off; the filtrate, diluted with water, was evaporated on the water bath to drive off the methyl alcohol and then acidified with sulfuric acid prior to ether extraction. Removal of the ether left an oil of honey-like appearance. On adding to it a mixture of ether and petroleum ether, a crystalline acid, m. pt. 276°, separated out. In view of the fact that fumaric acid melts with decomposition so that the literature data on its melting point vary widely, we converted the acid into its diphenacyl ester [9], m. pt. 197°. In admixture with an authentic specimen melting at 197.5° [10], the melting point was not depressed. On this evidence we can assume the presence of ethyl fumarate in fraction 7.

* In the literature [8] the m. pt. of trans-cyclopropane dicarboxylic acid is given as 175°.

Reaction of ethyl diazoacetate with allyl bromide*. Condensation of 79.05 g ethyl diazoacetate with excess allyl bromide (450 g) in presence of 0.5 g copper powder, followed by vacuum fractionation of the reaction product at 12 mm, gave two fractions: 1) 69-78°, 15.15 g; 2) 78-79°, 114 g.

As we have previously shown [1], fraction (2) is the ethyl ester of α-bromallylacetic acid. Examination of fraction (1) revealed the possibility of separating from it, by repeated fractionation at normal pressure, about 2 g of substance with high lachrymatory power, b. pt. 158-162°, at 760 mm; n_D^{16} 1.453.

Found %: Br 46.98. $C_4H_7O_2Br$. Calculated %: Br 47.84. Literature cited: b. pt. 158.2 at 760 mm [11], n_D^{13} 1.454 [12].

On the basis of the above constants and of the analytical data we may assume that the isolated bromide was not completely pure ethyl bromoacetate (this ester is known to be a strong lachrymator).

SUMMARY

1. It is shown that the reaction of ethyl diazoacetate with allyl chloride in presence of copper catalysts yields the ethyl esters of the following acids: chloracetic, α-chlorallylacetic, 2-(chlormethyl)-cyclopropane-1-carboxylic, and fumaric.

2. The structures were established of the esters (unknown in the literature) of α-chlorallylacetic and 2-(chlormethyl)-cyclopropane-1-carboxylic acids. The anilide of α-chlorallylacetic acid was prepared.

3. It is shown that the ester of 2-(chlormethyl)-cyclopropane-1-carboxylic acid does not isomerize to the ester of α-chlorallylacetic acid when heated with excess allyl chloride in presence of cuprous chloride.

4. In a further study of the ethyl diazoacetate-allyl bromide condensation, it was found that ethyl bromacetate is formed to a very slight extent.

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* See also [1]

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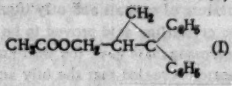
*** See Consultants Bureau translation, p. 2201.

REACTIONS OF ALIPHATIC DIAZO COMPOUNDS WITH UNSATURATED COMPOUNDS

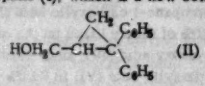
XII. CONDENSATION REACTIONS OF DIPHENYLDIAZOMETHANE AND ETHYL DIAZOACETATE WITH ALLYL ACETATE

I. A. Dyakonov and O. V. Guseva

Following up the papers by one of us on the reactions of ethyl diazoacetate [1] and diphenyldiazomethane [2] with allyl alcohol, we report here on the reaction of the same diazo compounds with allyl acetate. Diphenyldiazomethane readily reacts with boiling allyl acetate and, in contrast to the reaction with allyl alcohol, it forms one main reaction product- 1-(acetoxymethyl)-2,2-diphenylcyclopropane (I), which is a new compound.



(I)



(II)

The assignment of the acetate (I) to the cyclopropane series was confirmed by its conversion into the cyclic alcohol (II), previously prepared by one of us [2] from diphenyldiazomethane and allyl alcohol. The identity with the authentic specimen was established by comparison of their physical constants and by the determination of the mixed melting point of their 3,5-dinitrobenzoates. The yield of the analytically pure preparation of the acetate (I) was 55.25% of the theoretical yield. The chief losses of yield arise during vacuum rectification of the crude reaction product (the latter contains benzophenone which is not easily separated from the compound (V) by distillation. In the pure form benzophenone was only isolated in a yield of 3.5% of theory.* In place of the nearly colorless ketazine, there were separated from the crude condensation product two sorts of crystals with a yellow color: with m. pt. 157-158° and m. pt. 172-173°, the former predominating. Since the analytical data (nitrogen content, molecular weight) point to the crystals melting at 157-158° being the ketazine $C_{26}H_{20}ON_2$, and the melting point of a mixture with authentic ketazine [4] (m. pt. 162°) was not depressed, we are entitled to assume that the crystals in question are actually ketazine but contaminated with a substance of apparently similar composition. With the aim of determining the composition of this impurity, the crystals were hydrolyzed with 20-30% sulfuric acid when three hydrolysis products were obtained: Benzophenone, hydrazine sulfate and tetraphenylethane. According to Curtius (4) hydrolysis of authentic ketazine under the same conditions only gave two products – benzophenone and hydrazine sulfate:

$$(C_6H_5)_2C = N-N = C(C_6H_5)_2 \xrightarrow[H_2SO_4]{2H_2O} (C_6H_5)_2C = O + H_2N-NH_2 \cdot H_2SO_4$$

From the nitrogen content and the molecular weight, the crystals melting at 172-173° also correspond to $C_{26}H_{20}ON_2$, but the mixture with ketazine had the depressed melting point of 154-155°, and hydrolysis with sulfuric acid gave, in addition to benzophenone and hydrazine sulfate, twice as much tetraphenylethane as the same weight of crystals with m. p. 157-158°. The data suggest that the substance melting at 172-173° is actually the impurity in ketazine which caused the melting point to be depressed to 157-158° and which gave rise to tetraphenylethane among the hydrolysis products. The lack of material at our disposal prevented us from establishing the structure of this impurity which was isolated in the form of crystals with m. pt. 172-173°.

The reaction of ethyl diazoacetate with allyl acetate was performed, as customary, in presence of copper catalysts (anhydrous copper sulfate, copper bronze). The yield of the principal product of this reaction – the ethyl ester of 2-(acetoxymethyl)-cyclopropane-1-carboxylic acid – is 70.0% of the theoretical yield, but the crude

* According to Staudinger and co-workers [3] benzophenone is a very minor product of the decomposition of diphenyldiazomethane.

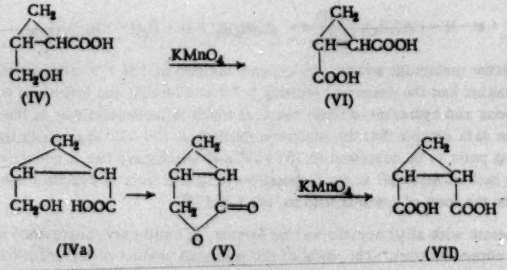
preparation contains a small admixture of ethyl fumarate which could not be completely removed by fractional distillation.

The ester (III) (yield 62.7% of theory calculated on the ethyl diazoacetate) was obtained in the perfectly pure form after treatment of the crude ester with cold potassium permanganate solution. Among the oxidation products was oxalic acid, which by analogy with previous investigations in this field was assumed to be proof of the formation of ethyl fumarate. A rough calculation based on the consumption of oxidizing agent shows that the ethyl fumarate content of the crude ester (III) does not exceed 3% of the weight of (III). The constants of the crude preparation likewise only differ slightly from those of the purified ether (III).

Measurement of the Raman spectra* of the ester (III) (see experimental part) confirmed the presence of the cyclopropane nucleus. In accordance with the literature data on this subject (for literature see Comm. VII of this series) the frequencies 862 (2), 1202 (3) are characteristic of the disubstituted cyclopropane ring. For the carbonyl group of the ester (III) the frequency 1729 (3) was found. Alkaline hydrolysis of ester (III) gave the corresponding 2-hydroxymethylcyclopropane-1-carboxylic acid (IV) in the form of a mixture of crystals and oily liquid. The yield of crude acid (IV) is 80% of theory based on the original ester (III). The crystalline acid proved to be the trans-isomer of the cyclic hydroxy acid (IV), since oxidation with potassium permanganate gave the well-known trans-cyclopropane-1,2-dicarboxylic acid (VI) in 84.6% yield. Our further research revealed that the oily acid was a mixture of trans- and cis-hydroxymethylcyclopropane carboxylic acids. Careful vacuum distillation of this mixture resulted in cleavage of water from the cis-acid (IVa) with formation of a bicyclic lactone (V) which we have isolated and characterized. The trans-isomer of the acid (IV) was obtained by crystallization of the undistilled residue.

The lactone ring of (V) is easily opened under the action of caustic alkali solutions and is converted by permanganate oxidation into cis-cyclopropane-1,2-dicarboxylic acid (60% yield). These reactions determine its structure. In addition, measurements of the Raman spectra** are in harmony with the formula (V). The presence of the trimethylene ring is indicated by the frequencies 850 (9), 1171 (7), 2981 (4), 3002 (5) and 3085 (8).*** A conspicuous feature is the displacement into the long-wave region of the spectrum of the first two of the above-mentioned lines, which must undoubtedly be ascribed to the influence of conjugation with the cyclopropane 5-membered ring. To the latter corresponds the frequency 899 (4). The frequency of the carbonyl group of the lactone (1760 cm^{-1}) slightly exceeds the frequency of the carbonyl group in other compounds (1730 cm^{-1}).

On the basis of the amount of lactone (V) obtained, the yield of cis-isomer of the acid (IVa) in the hydrolysis reaction is only 7% of the theoretical. The yield of trans-isomer (IV) is 55.7% of the theoretical. We may assume that the corresponding stereoisomeric forms of ester (III) will also occur in the same ratio (1:8).



Of the compounds described above, three have been prepared for the first time: the cyclic ester (III), the trans-isomer of the hydroxy acid (IV) and the bicyclic lactone (V).

EXPERIMENTAL

I. Condensation of diphenyldiazomethane with allyl acetate. Starting materials were: a) Allyl acetate prepared by the method of Swanson and Coss [6]. B. pt. 103-104.5°; d_4^{17} 0.9277; n_D^{17} 1.4047. (Literature data:

* Measurements were performed by A.P.Ryskalchuk to whom the authors convey their thanks.

** All measurements and calculations were performed by M.E.Shmulyakovsky to whom we express our deep gratitude.

*** The remaining frequencies are enumerated in the experimental part.

b. pt. 103.5-104°; d_4^{18} 0.9279; n_D^{19} 1.4048. No active hydrogen was found, indicating absence of allyl alcohol (b. pt. 97°). b) Diphenyldiazomethane was prepared as in [5].

Synthesis. Into a reaction flask fitted with a reflux condenser and a dropping funnel was introduced 75 ml allyl acetate, and in the dropping funnel was placed 33-33 g diphenyldiazomethane mixed with the same volume of allyl acetate. The diphenyldiazomethane is slowly added dropwise to the boiling allyl acetate.

The reaction is accompanied by evolution of nitrogen and change of color of the solution. Towards the end of the experiment the color of the solution changes from dark-red (the color of diphenyldiazomethane) to light yellow. In the manner described, separate portions of diphenyldiazomethane, totalling in all 216.6 g, were reacted. At the end of the reaction the solutions from the individual experiments were combined and the excess allyl acetate distilled off in a 150 mm vacuum. The residue in the distillation flask was diluted with cold ethyl alcohol; at this point it was noted that deep-colored crystals first separated with an m.pt. of 165-170° (2.2 g). Further dilution of the reaction product with ethyl alcohol (up to 10-12 times the volume) led to crystallization of not so deeply colored crystals. The total amount of the latter was 12.5 g. M. pt. 152-155°. After several recrystallizations from alcohol and from alcohol-benzene mixture, the first portion of cyrstals melted at 172-173°; the second portion, after recrystallization from the same solvents, had the raised m. pt. of 157-158°. See below for further details of the examination of the crystals with m.pt. 172-173° and 157-158°.

The alcoholic mother liquor from the crystals, containing in solution the main reaction product, was subjected to distillation in vacuum at 25-30 mm to drive off the alcohol, and the residue (a dark, viscous oil) was fractionated in vacuum (0.5 mm). As the result of a series of repeated fractional distillations, the condensation product which had first come over in a wide temperature range was separated into the following fractions (at 0.5 mm): First fraction 107-120°, n_D^{16} 1.594, 8 g; second fraction, 120-135°, n_D^{16} 1.591, 6 g; third fraction, 135-150°, n_D^{16} 1.578-1.568, 15 g; fourth fraction, 147-150°, n_D^{16} 1.564, 163.7 g.

On the basis of further studies, the fourth (main) fraction was taken to be the cyclic acetate (I); the first and second fractions were considered to be a mixture of benzophenone and the acetate (I); the third fraction was apparently an intermediate one; it was resolved by further distillation into a series of separate subfractions whose refractive indices varied within the above-stated limits. The yield of pure acetate (I) was 163.7 g or 55.25% of the theoretical

The most sensitive measure of the purity of acetate (I) proved to be the refractive index and not the boiling point. The entire distillation process was therefore checked by the value of n_D of the individual fractions. For the fourth fraction or acetate (I) a constant n_D was obtained which did not change after the second distillation. In the case of the remaining fractions it was impossible to attain a constant n_D due to the smallness of the quantities.

II. 1-(Acetoxymethyl)-2,2-diphenylcyclopropane (I). The freshly distilled preparation was a fairly viscous, light-yellow oil; the viscosity was higher than that of the corresponding alcohol (II). It turns a deeper yellow in storage while the refractive index increases slightly. B. pt. 165-167° (2 mm); 147-150° (0.5 mm); $d_4^{20.5}$ 1.0914; n_D^{20} 1.5620; MR_D 79.12; calculated 78.28. Exaltation 0.84.

0.1409 g substance: 0.4180 g CO_2; 0.892 g H_2O. 0.3176 g, 0.3181 g substance; 16.01 g, 16.64 g benzene: Δt 0.37, 0.37°. Found %: C 80.93; H 7.08; M 275.1, 264.3. $C_{18}H_{18}O_2$. Calculated %: C 81.19; H 6.84; M 266.3.

Hydrolysis of acetate (I). A mixture of 17 g potassium hydroxide dissolved in 90 ml methyl alcohol with 52.5 g acetate (I) was heated for 1½ hours on the water bath under a reflux condenser. The excess alkali was neutralized with carbon dioxide, the potassium carbonate was filtered off, and the methyl alcohol distilled off in vacuum. The flask residue was dissolved in ether and the ethereal solution was washed with water and dried with calcium chloride. The very viscous yellow oil remaining after removal of the solvent was distilled in vacuum: B. pt. 165-167° (3.5 mm); n_D^{21} 1.583. The 3,5-dinitrobenzoate melted at 140° and did not depress the m. pt. of the 3,5-dinitrobenzoate of the cyclic alcohol (II) (m. pt. 140°) described by one of us [2]. Yield of alcohol (II) in the hydrolysis reaction was 37.0-38.8 g or 83.8-87.8% of the theoretical.

III. Investigation of the by-products of the reaction of diphenyldiazomethane with allyl acetate. Benzophenone. The opaque, dirty-white first and second fractions of the condensation product with n_D^{16} 1.594-1.591 partly crystallized on keeping. The crystals were filtered off and sucked free from the residual uncrystallized portion (5.9 g) which was a transparent, colorless oil with n_D^{16} 1.5745 (compare n_D^{16} for the third fraction in section I above). The crystals melted at 43-46°, and after one recrystallization from alcohol they melted at 48-49°.

They were identical with authentic benzophenone (mixed melting test). Yield 7.35 g or 3.5% of theory, calculated on the original diphenyldiazomethane.

The crystals melting 157-158° had a light-yellow color and were difficultly soluble even in hot alcohol, easily soluble in ether, and still more easily in benzene. It was impossible to raise the melting point either by repeated crystallizations from alcohol-benzene or by substitution of solvent (benzene, ether). Nitrogen determinations, however, gave results corresponding to the formula for ketazine and a mixed sample with authentic ketazine (m. pt. 162°) melted without depression (at 160°).*

Found %: N 7.95, 7.62; M 366.2. $C_{26}H_{22}N_2$. Calculated %: N 7.78; M 360.3.

Hydrolysis of the crystals melting at 157-158° with sulfuric acid. 1 g of the substance and 150-200 ml 20-30% sulfuric acid were boiled for many hours under a reflux condenser until the crystals had gone completely into solution. The solution (with a thin layer of yellow oil floating on its surface) was then steam-distilled. From the distillate of the ether extraction was obtained 0.57 g (57% of theory**) benzophenone with m. pt. 46-47°, which rose after recrystallization from alcohol to 48-49° and did not depress the m. pt. of an authentic sample. The solution remaining in the distillation flask was filtered from a small amount of solid precipitate which, after drying, weighed 0.16 g and melted at about 206°. This solid was very difficultly soluble in alcohol and rather more soluble in benzene. After crystallization from alcohol-benzene it melted at 207.5°. This melting point remained constant.

Hydrolysis (in the above-described manner) of the crystals melting at 157-158° with 20% sulfuric acid gave 0.75 g of slightly yellowish crystals melting at 207.5° (after one crystallization from alcohol-benzene). Further crystallization gave 0.63 g of colorless crystals with the same melting point. A qualitative test for nitrogen by Lassaigne's method gave a negative result, while analysis gave results fairly close to those calculated for tetraphenylethane (the literature gives m. pt. 209° [7]).

Found %: C 92.90, 92.92; H 6.68, 6.93. $C_{26}H_{22}$. Calculated %: C 93.14; H 6.86.

For comparison, authentic tetraphenylethane was prepared by the action of granulated zinc on diphenylbromomethane dissolved in dry ethylacetoacetate [8]. M. pt. 206°. No depression of melting point when mixed with the investigated preparation.

The sulfuric acid filtrate from the tetraphenylethane prepared by hydrolysis of 1 g crude ketazine with m. pt. 157-158° was concentrated on the water baths, and then cooled to separate 0.1 g hydrazine sulfate with m. pt. 254-258° (with decomposition) [4]; yield 28% of theory based on the formula of ketazine.

Hydrolysis of authentic ketazine. Heating of 1 g ketazine (m. pt. 162°) in 30% sulfuric acid gave benzophenone with m. pt. 48-49° (0.59 g or 59% of the theoretical yield) and hydrazine sulfate with m. p. 255° with decomp.) (0.31 g or 86% of theory). Tetraphenylethane was not found among the hydrolysis products. The same data (without indication of yields) were reported by Curtius [4].

Crystals with m. pt. 172-173°. As already pointed out in section I above, crystals melting at 172-173° were obtained after 2-3 recrystallizations of the substance, separating in the first operation, on dilution of the crude condensation product with alcohol. Weight 1.4 g. After crystallization, the color of the crystals and the solubility were approximately the same as those of the crystals with m. pt. 157-158°. A mixed sample with authentic ketazine (m. pt. 162°) gave a depression of m. pt. (154-155°). Determinations of nitrogen and of the molecular weight did not permit a choice to be made between the formulas $C_{26}H_{22}N_2$ and $C_{26}H_{24}N_2$:

0.1220 g substance: 8.15 ml N_2 (18°, 744 mm). 0.1085 g substance; 9.39 g benzene; Δt 0.170°. Found: % N 7.85; M 349.4. $C_{26}H_{22}N_2$. Calculated %: N 7.73; M 362.3. $C_{26}H_{24}N_2$. Calculated %: N 7.78; M 360.3.

Hydrolysis of the crystals with m. pt. 172-173°. After heating with 30% sulfuric acid, 1 g of substance yielded 0.42 g benzophenone with m. pt. 43-44° (not recrystallized), 0.35 g tetraphenylethane with m. pt. 207° (not recrystallized) and 0.07 g hydrazine sulfate.

IV. Condensation of ethyl diazoacetate with allyl acetate. Ethyl diazoacetate was purified by distillation with steam. The catalyst, copper sulfate, was dehydrated at 170-180°. Into a round-bottomed flask, fitted with a mercury seal and stirrer, a dropping funnel and a reflux condenser, was charged 380 ml allyl acetate and 2 g anhydrous copper sulfate; in the dropping funnel was placed a solution of 136.9 g ethyl diazoacetate in 136 ml allyl acetate. The allyl acetate in the flask was heated to boiling, after which with energetic stirring the solution in the

* Authentic ketazine was prepared by the action of iodine in alcoholic solution on benzophenone hydrazone [4].

** Calculated on the gross formula of $C_{26}H_{22}ON_2$ for the substance melting at 157-158°.

dropping funnel was slowly added. Even after only a few drops had been run in, the contents of the flask turned grey; with further addition the color changed to nearly black. The nitrogen evolved during the reaction was collected in a gasholder. At the end of the experiment 25.24 l nitrogen (normal conditions) had been collected, equivalent to 93.8% of the theoretical amount. After 20-30 minutes the evolution of nitrogen usually ceased (indication of end of reaction). After cooling and filtering off the catalyst, the excess allyl acetate was distilled off from the solution in vacuum (130 mm). The residue in the distillation flask was distilled in a 1 mm vacuum. Nearly the whole of the condensation product came over within the range of 83-86° at 1 mm. Yield 57.7 g or 70.6% of theory, calculated on the formula of ester (III), $C_9H_{14}O_4$. B. pt. 111-114° (10 mm); 92-95° (3 mm); 83-85° (1 mm); $d_4^{18.9}$ 1.078; d_4^{18} 1.079; $n_D^{18.9}$ 1.4422; n_D^{18} 1.4431.

0.1422 g substance: 0.3173 g CO_2; 0.1060 g H_2O. Found %: C 58.00; H 7.94. $C_9H_{14}O_4$. Calculated %: C 58.06; H 7.57.*

With the aim of reducing the amount of resin in the reaction products, we tried to perform the reaction at a temperature much below the boiling point of allyl acetate, but without success. Thus in one experiment the ethyl diazoacetate was run in at a reaction mixture temperature of 65-70°. In this case nitrogen, as a rule, was not evolved, and the solution retained its yellow-green color, indicating the presence of undecomposed ethyl diazoacetate. After a few grams of ethyl diazoacetate had been added to the solution, for no apparent reason a violent and exothermic decomposition of the diazoacetate set in, accompanied by ejection of part of the solution through the seal and condenser. The temperature of the solution suddenly rose to 103° and the color darkened.

183 g crude ester (III) was treated in the cold with 3% potassium permanganate (14.9 g) until the violet color of the solution had disappeared. After filtration of the manganese dioxide, which was carefully washed with ether, the ester (III), separating as a colorless oil in the filtrate, was separated from the aqueous layer and the latter was extracted with ether. The combined ether extracts were mixed with ester (III), the solution dried with $CaCl_2$, and after driving off the solvent the ester (III) was distilled in vacuum. Yield of analytically pure preparation 162.9 g (88.7% of theory). B. pt. 128-129° (22 mm); 106-107° (8 mm); 76-77° (0.5 mm); $d_4^{18.8}$ 1.079; $n_D^{18.8}$ 1.4429; MR_D 45.74; calculated. 44.85; exaltation: 0.19.

0.2272 g, 0.1117 g substance: 0.4888 g, 0.2373 g CO_2; 0.1587 g, 0.0767 g H_2O. Found %: C 58.19, 57.95. H 7.82, 7.68. $C_9H_{14}O_4$. Calculated %: C 58.06; H 7.57. 0.1836 g, 0.1851 g substance: 16.82 g, 22.96 g benzene; Δt 0.300°, 0.225°. Found: M 186.7, 183.9. $C_9H_{14}O_4$. Calculated: M 186.2.

Raman spectrum of ester(I) was measured with the help of a Zeiss triprism spectrograph, using a mercury lamp (wave length λ 4358.3 A) as source of excitation; slit 0.1 mm; time of exposure 6 hours. Light filter: hard glass. Results of measurements of spectrum of ester (III): 636.4 (3), 746(3), 840.9(1), 862.2(2), 889.7(2), 1033.4(2), 1098.9(2), 1118.5(2), 1202.9(3), 1455(5), 1728.7(3), 2948(5), 3137(4).

The manganese dioxide obtained during the oxidation was twice extracted with boiling water and the wash liquors combined with the aqueous solution previously separated from the layer of purified ester (III). From the combined solutions the volatile and volatile-in-steam organic acids were separated in the usual manner. The aqueous distillate contained 0.95 g (estimated by alkali titration) of acid and in the solution of nonvolatile acids was found 3 g of oxalic acid whose identity was confirmed by analysis of the calcium salt.

Found %: Ca 27.70, 27.45. $C_2O_4Ca \cdot H_2O$. Calculated %: C 27.30.

VI. Trans-2-(hydroxymethyl)-cyclopropane-1-carboxylic acid (IV). Saponification of the cyclic ester (III) for the purpose of preparing 2-hydroxymethyl-cyclopropane carboxylic acid was effected by various methods, including the action of a methyl alcoholic solution of potassium hydroxide, the action of aqueous solutions of potassium hydroxide, and the action of barium hydroxide. The best yields could be obtained by the following procedure.

Into a three-liter round-bottomed flask fitted with a stirrer and a reflux condenser was charged 186 g (1 mole) cyclic ester (III) and 1400 ml of 2N solution of potassium hydroxide. The reaction mixture was boiled with stirring until the originally turbid solution had become transparent. After cooling, the excess of alkali was neutralized to phenolphthalein with 2 N sulfuric acid (the ratio of the volumes of solutions of alkali and acid determined by titration to phenolphthalein was 25 ml 2N KOH to 20.2 ml of 2 N H_2SO_4). 66 ml of 2 N H_2SO_4 was consumed,

* If we assume that 3% ethyl fumarate is contained in ester (III), then the calculated C and H contents of the crude preparation are respectively 57.93 and 7.48%.

equivalent to 82 ml of 2N solution of excess KOH. The neutral solution was then concentrated on the water bath to a volume of about 300 ml, and to this solution was added 1000 ml 2N H_2SO_4 – an amount nearly sufficient for complete separation in the free state of both of the organic acids (the theoretical requirement is 1065 ml 2N H_2SO_4). The acidified solution was concentrated in vacuum to a volume of 200 ml prior to removal by steam-distillation of the main bulk of ethyl acetate formed in the hydrolysis. The residue of acetic acid was removed from the solution by steam-distillation at the ordinary pressure. The solution was then acidified for the last time (70-100 ml 2N H_2SO_4) and transferred to a Soxhlet apparatus for ether extraction of the cyclic acid.

After extraction for several days (the acid is sparingly soluble in ether and readily soluble in water), the ether was evaporated off and the residual oily acid was kept in a vacuum, first at room temperature and then at 50-60°; in this way the remaining ether, water and acetic acid were removed. The acid dried in this manner is a pale-yellow, very viscous oil. Yield 92.8 g or 80% of theory calculated on the ester (III). On prolonged standing in the desiccator it gradually crystallizes, but not completely, a portion remaining as an oil. In the experiment here described, the crystallized acid was filtered off at the pump to get rid of the oil and the crystals washed on the filter with a small quantity of cold ether. After keeping on a porous porcelain plate the crystals were freed from the last traces of adsorbed oil. The solid acid was a white, bulky powder melting at 63°. Weight 57.6 g. By the method described blow the separated oil yielded a further 7 g solid acid melting at 62-64°. Consequently the total yield of crystalline trans-(2)(hydroxymethyl)-cyclopropane-1-carboxylic acid was 64.6 g or 55.7% of theory. The acid was obtained in the analytically pure form after a single recrystallization from a mixture of ether and petroleum ether. M. pt. 64-65°.

0.2794 g, 0.1761 g substance: 32.3 ml, 20.3 ml 0.1 N. NaOH (factor 0.7456). 0.1301 g, 0.1312 g substance: 0.2459 g, 0.2495 g CO_2; 0.0830 g, 0.0846 g H_2O. Found. equiv. 116.1% C 51.72; H 6.94.

Oxidation of acid (IV). 5.8 g (0.05 mole) of acid, dissolved in a little water, was treated in the cold with the calculated amount (10.5 g = 0.066 mole) of potassium permanganate used in the form of 30% solution. After working up in the usual manner, the aqueous solution of the oxidation products was concentrated to a volume of 40-50 ml, acidified with 3 ml concentrated sulfuric acid, and extracted with ether in the Soxhlet.

The ether extract yielded 5.5 g (84.6% of theory) of crystalline trans-2-cyclopropane-1,2- dicarboxylic acid with m. pt. 173° (175° after crystallization from water), in agreement with the literature [7].

Found %: C 46.32; H 4.99; equiv. 64.89, 64.88. $C_5H_6(CO_2H)_2$. Calculated %: C 46.17; H 4.75; equiv. 65.05.

There was no melting point depression in admixture with a preparation of the same acid obtained by another route [1].

VII. Lactone of cis-2-(hydroxymethyl)-cyclopropane-1,2-dicarboxylic acid (V). 28 g of the oily acid filtered off, as above, from the solid acid (IV), was subjected to supplementary drying by keeping in a 10 mm vacuum, first at 60° and then at 90°. This operation likewise failed to cause crystallization. An attempt was then made to distil the liquid acid in a 2 mm vacuum. This distillation yielded (from 24 g liquid acid) 7.1 g of colorless distillate boiling at 62-72° (1.5-2.5 mm), leaving 16.3 g residue which crystallized on standing. Pressing on a porous plate followed by recrystallization from ether-petroleum ether mixture gave 7 g of trans-2-(hydroxymethyl)-cyclopropane-1-carboxylic acid with m. pt. 62-64°. Following a second distillation, the main portion of the distillate had b. pt. 66-70° (2 mm) and its analysis corresponded to that of lactone (V): d_4^0 1.199; d_4^{20} 1.180; n_D^{20} 1.4652; MR_D 23.00; calculated 23.24.

0.1464 g, 0.1340 g substance: 0.3278 g, 0.3055 g CO_2; 0.0824 g, 0.800 g H_2O. 0.1654 g, 0.2074 g substance; 17.17 g, 16.70 g benzene: Δt 0.47°, 0.60°. Found %: C 61.05, 60.81; H 6.30, 6.53; M 105.4, 106.4. $C_5H_6O_2$. Calculated %: C 61.22; H 6.17; M 98.1.

The lactone is not attacked by 0.1 N caustic alkali solution on momentary contact. In the cold the alkali is slowly consumed; on heating with excess 0.1 N alkali solution the lactone ring is quickly ruptured. Below are presented data for molecular weight determination of lactone (V) by the back-titration method (using phenolphthalein): 0.1803 g, 0.1784 g substance: 50 ml, 50.2 ml 0.1 N. NaOH (factor 0.7285); 16.35 ml, 16.70 ml 0.1 N. HCl (factor 1.083). Found: M 96.36, 96.61. $C_5H_6O_2$. Calculated: M 98.11.

Raman spectrum of lactone (V): 185(6), 243(4), 378(4), 478(5), 558(1), 613(9), 648(2), 705(10), 780(6), 829(5), 850(9), 899(4), 952(8), 975(6), 994(4), 1038(2), 1055(2), 1112(3), 1171(7), 1220(2), 1309(3), 1344(4), 1373(1), 1450(3), 1481(4), 1760(6W), 2910(5), 2981(4), 3002(5), 3085(8).

The spectrum of the lactone was recorded with an ISP-51 triprism spectrograph. Slit width 0.04 mm. Exposure period 6 hours. Glass light filter; Hg 436. Intensities were evaluated photometrically.

Oxidation of lactone (V). To 3.95 g (0.04 g-mole) lactone was added a solution of 2.25 g (0.04 g-mole) potassium hydroxide in 20 ml of water, and the resultant solution of potassium salt of acid (IVa) was treated, first in the cold and then on the water bath, with the calculated amount (8.45 g) potassium permanganate in the form of a 3% solution. After working up in the usual manner, the cis-cyclopropane-1,2-dicarboxylic acid was separated from the acidified solution by ether extraction. Yield 3.12 g (0.024 g-mole, 60% of the theoretical yield). After two crystallizations from water it melted at 138-139° [9].

Found %: C 45.90, 45.77; H 4.77, 5.01; equiv. 65.75, 65.67. $C_3H_6(CO_2H)_2$. Calculated %: C 46.17; H 4.65; equiv. 65.05.

SUMMARY

1. It is shown that reaction of diphenyldiazomethane with allyl acetate results in a 55% yield of 1-acetoxymethyl-2,2-diphenylcyclopropane, which on alkaline hydrolysis gives the previously investigated 1-hydroxymethyl-2,2-diphenylcyclopropane.

2. By-products of the first-mentioned reaction are benzophenone, ketazine (tetraphenylazimethylene) and a product of similar structure to ketazine which on alkaline hydrolysis yields tetraphenylethane, benzophenone and hydrazine sulfate.

3. Rreaction of ethyl diazoacetate with allyl acetate in presence of copper sulfate leads to formation in 70% yield of 2-(acetoxymethyl)-cyclopropane-1-carboxylic acid together with an insignificant amount of ethyl fumarate.

4. Alkaline hydrolysis of 2-(acetoxymethyl)-cyclopropane-1-carboxylic acid is shown to yield a mixture of the trans- and cis-forms of the corresponding cyclic hydroxy acid; the trans-isomer can be isolated from the mixture, and the cis-form can be converted into the lactone by heating.

5. By oxidation of the trans-isomer of the acid it is possible to obtain transcyclopropane-1,2-dicarboxylic acid in a yield of 84% of theory; oxidation of the lactone gives the cis-form of the acid in 60% yield.

6. The structures of the cyclic ester and of the bicyclic lactone were confirmed by data for the Raman spectra of these compounds.

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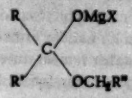
STERIC HINDRANCE IN ORGANOMAGNESIUM REACTIONS

XII. THE REACTION OF DIMETHYL OXALATE WITH DI-ortho -SUBSTITUTED ARYL MAGNESIUM HALIDES

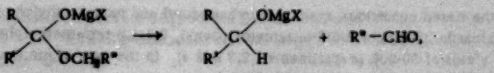
I. I. Lapkin, N. K. Ponomareva and L. Yu. Pinegina

In a previous communication [1] a study was made of the cause and mechanism of the reductive reactions which take place when esters react with organomagnesium compounds.

The stability of the initially formed compound



depends both on the character of the radicals R and R' and on the character of the alkoxyl group. The more electrophilic are radicals R and R', the less stable is the compound. The stability may be reduced to such an extent on heating at 40-42° (the boiling point of the ethereal solution) that the compound decomposes according to the equation:



which also involved reduction. The decomposition is naturally possible if the esters are formed with primary and secondary alcohols. Thus the esters of oxalic acid containing both primary and secondary alkoxyl groups form esters of secondary α-hydroxy acids [2,3] on reacting with ortho-substituted aryl magnesium halides and with branched alkyl magnesium halides.

As was pointed out in the same paper [1], the only exception is the dimethyl ester of oxalic acid which when reacted with equivalent amounts of di-ortho-substituted aryl magnesium halides forms methyl esters not of α-hydroxy acids but the normal products of the first stage of the reaction—methyl esters of α-keto acids.

This difference, however, is not fundamentally significant, as will be demonstrated in the present paper. The difference only resides in the higher thermal stability of the magnesium complex formed with the above compounds; its decomposition calls for a much higher temperature (100°).

Under these conditions dimethyl oxalate and methyl magnesium bromide form the methyl ester of 2,4,6-trimethylmandelic acid (experiment 1). Under the stated conditions dimethyl oxalate and duryl, isoduryl and pentamethylphenyl magnesium bromides similary react to form, respectively (experiments 2,3,4), the methyl esters of 2,3,5,6-tetramethyl, 2,3,4,6-tetramethyl and pentamethylmandelic acids (I).

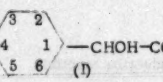
In connection with the reaction of the methyl ester of oxalic acid with sterically hindered organomagnesium compounds, we must take account of still another feature—the occurrence in large measure of saponification which results in the formation of a relatively large amount of magnesium oxalate.

In general, as shown previously (1,2), the formation of esters of secondary α-hydroxy acids with the help of esters of oxalic acid is nearly always accompanied to some degree by the side reaction of saponification of these esters, probably in accordance with the equation put forward by Stadnikov [4] and Zalkind [5]. The possibility is not excluded of saponification proceeding by another route, similar to the alkylation of esters with sulfuric acids and sulfo acids. Cases are even known of the formation of esters of organic acids by such a method. For example, Gilman and Robinson [6] found that allyl benzoate and phenyl magnesium bromide

form a small quantity of allylbenzene, while Arnold [7] obtained 57% of allylmesitylene with the help of the same ester.

With the majority of the esters of oxalic acid the saponification reaction proceeds to a minor degree, but with diphenyl and dimethyl esters this side reaction becomes the principal one. Experiments with various esters of oxalic acid and mesityl magnesium bromide have yielded the following esters with the degrees of saponification shown: Diphenyloxalate – 80%; dimethyl oxalate – 40%; diethyl oxalate – 16%; di-n-butyl oxalate – 10%; diisobutyl oxalate – 9%; diisopropyl oxalate – 6%.

The above figures show that the degree of saponification depends on the character of the radicals of the alkoxyl group entering into the composition of the oxalic acid esters. The more electronegative is the radical, the greater the degree of this reaction. The radicals concerned can thus be arranged in the following order of electronegativity:



(I)

$C_6H_5- > CH_3- > C_2H_5- > n\text{-}C_4H_9- > iso\text{-}C_4H_9- > iso\text{-}C_3H_7-$.

This order agrees entirely with that of Norris [8] and Kharasch [9].

The saponifying tendency of the methyl and phenyl esters of oxalic acid can be exploited for the development of a rather interesting method of synthesis of di-ortho-substituted arylglyoxalic acids. Although magnesium oxalate does not, as our experiments showed, react with aryl magnesium halides either under the usual temperature conditions employed for organomagnesium reactions or at much higher temperatures (100°), it was to be expected that at the instant of its formation this salt would be more active and on reaction with di-ortho-substituted aryl magnesium halides it would form the magnesium salt of the arylglyoxylic acids.

The formation of arylglyoxylic acids might be explained by the possibility of saponification of the already formed esters of the arylglyoxylic acids with magnesium bromide, but this possibility is ruled out because it has been experimentally shown that esters of mesitylglyoxylic acid are not saponified by magnesium bromide at 100°.

With dimethyl oxalate under the stated conditions, mesityl, duryl, isoduryl and pentamethylphenyl magnesium bromides form, respectively, 2,4,6-trimethylphenyl, 2,3,5,6-tetramethylphenyl, 2,3,4,6-tetramethylphenyl and pentamethylphenylglyoxylic acids with yields of 30-20% (experiments 1,2,3 and 4). In the case of monosubstituted aryl magnesium halides it was not found possible to effect the reaction in such a manner.

Consequently, three products are formed by reaction of dimethyl oxalate with di-ortho-substituted aryl magnesium halides at an elevated temperature (100°): Methyl esters of arylglycolic acids, arylglyoxylic acids, and the magnesium salt of oxalic acid. In view of the fact that the arylglyoxylic acids are obtained in a fairly pure form, the method can be recommended for the preparation of these acids.

EXPERIMENTAL

1. Reaction between mesityl magnesium bromide and dimethyl oxalate at high temperature (ratio of 1:1). To a solution in ether of 30 g dimethyl oxalate (0.25 mole) is gradually added an ethereal solution of mesityl magnesium bromide prepared from 50 g mesityl bromide (0.25 mole) and 6.5 g magnesium. After the mixing of the reaction components the ethyl ether was replaced by toluene and the reaction mixture then heated for 20 hours on a boiling water bath, after which it was decomposed with water and 10% hydrochloric acid. Following the removal of the aqueous layer, the toluene solution was washed with water, with 10% sodium carbonate and again with water until the reaction was neutral, and then dried with calcined sodium sulfate. Finally, after distilling off the toluene, the residual mixture of substances was distilled in vacuum. The main fraction (130-145° at 6 mm, 6 g) was dissolved in petroleum ether (boiling up to 70°) and cooled. The separated crystals of the methyl ester of 2,4,6-trimethylmandelic acid were purified by recrystallization from the same solvent until the m. pt. was constant at 90-91°.

0.1076 g substance: 0.2722 g CO_2; 0.0757 g H_2O. Found %: C 69.23; H 7.89. $C_{12}H_{16}O_3$. Calculated %: C 69.22; H 7.75. 0.1678 g substance: 18.3 ml CH_4 (20°, 754 mm). Found %: OH 7.6. $C_{12}H_{16}O_3$. Calculated %: OH 8.1.

The literature [10] gives the m. pt. of the ester as 90-91° and 91-92°.

The soda solution was washed twice with ether and then acidified with hydrochloric acid; the resultant yellow crystals of 2,4,6-trimethylphenylglyoxylic acid were washed with cold water, dried, and purified by a single recrystallization from petroleum ether-toluene mixture. M. pt. 115-116°. Yield 12.5 g (25%).

0.1153 g substance: 0.2915 g CO_2; 0.0665 g H_2O. Found %: C 68.99; H 6.45. $C_{12}H_{16}O_3$. Calculated %: C 68.71; H 6.30. 0.1939 g substance: 23.6 ml CH_4 (20°, 754 mm). Found %: active H 0.50. $C_{12}H_{16}O_3$. Calculated %: active H 0.52.

In the literature [10] this acid is stated to melt at 116, 118°.

An increased yield of this acid did not result from raising the temperature of heating of the reaction mixture to 140°.

2. Reaction between duryl magnesium bromide and dimethyl oxalate at a high temperature (ratio 1:1). As in the preceding experiment, addition to the ether solution of dimethyl oxalate was made of an ether solution of duryl magnesium bromide (0.1 mole) prepared under the previously described conditions [2]. After the reactants had been mixed the ether was replaced by toluene and the mixture heated on the boiling water bath for 20 hours. Decomposition of the magnesium complex was effected with water and 20% hydrochloric acid. Treatment of the toluene layer (10%) with soda solution brought down the sodium salt (sparingly soluble in water) of 2,3,5,6-tetramethylphenylglyoxylic acid which was filtered off, washed with ether and dried.

Decomposition of this salt with 10% hydrochloric acid yielded light-yellow crystals of 2,3,5,6-tetramethylphenylglyoxylic acid (7.5 g, 36% yield), which were washed with water and dried prior to purification by recrystallization from a mixture of petroleum ether and toluene until the melting point was constant at 125-126°.

0.1097 g substance: 0.2802 g CO_2; 0.0676 g H_2O. Found %: C 69.69; H 6.90. $C_{12}H_{14}O_3$. Calculated %: C 69.88; H 6.84. 0.1297 g substance: 14.2 ml CH_4 (17.5°, 762 mm). Found %: active H 0.48. $C_{12}H_{14}O_3$. Calculated %: active H 0.48.

A m. pt. of 124° is reported for 2,3,5,6-tetramethylphenylglyoxylic acid in the literature [10].

The toluene solution was washed with water and dried. Distillation gave a fraction (2.75 g) at 145-165° at 8 mm which was dissolved in an equal amount of petroleum ether and cooled. The resultant crystals of the methyl ester of 2,3,5,6-tetramethylmandelic acid were purified by further recrystallization from the same solvent until the melting point was constant at 119-120°.

0.1173 g substance: 0.3010 g CO_2; 0.0861 g H_2O. Found %: C 76.02; H 8.21. $C_{13}H_{18}O_3$. Calculated %: C 70.24; H 8.16. 0.1245 g substance: 11.6 ml CH_4 (17.5°, 766 mm). Found %: OH 6.74. $C_{13}H_{18}O_3$. Calculated %: OH 7.60.

This ester has not been described in the literature.

3. Reaction of dimethyl oxalate with duryl magnesium bromide at high temperature (ratio of 1:1). This reaction was performed with the same amounts of components (0.25 mole each) and under the same conditions as in experiment 1.

After distillation, from the toluene solution was obtained a fraction (4 g) at 140-185° (11 mm).

A narrower cut of this fraction (155-165° at 11 mm) was collected (3 g). It was dissolved in petroleum ether and cooled. The separated crystals of the methyl ester of 2,3,4,6-tetramethylmandelic acid were purified by recrystallization. M. pt. 80-81°.

0.1201 g substance: 0.3081 g CO_2; 0.0869 g H_2O. Found %: C 70.01; H 8.10. $C_{13}H_{18}O_3$. Calculated %: C 70.24; H 8.16.

There was separated from the soda solution, by the previously described method, liquid 2,3,4,6-tetramethylphenylglyoxylic acid in the amount of 14 g (25%). Reduction of this acid with sodium amalgam in aqueous alcoholic solution yielded 2,3,4,6-tetramethylmandelic acid with m. pt. 153°. The literature [10] gives 156°.

4. Reaction of dimethyl oxalate with pentamethylphenyl magnesium bromide at high temperature (ratio of 1:1). Since neither pentamethylphenyl bromide nor the dibromide reacted completely with magnesium, the ether solution of pentamethylphenyl magnesium bromide was prepared under the previously described conditions [2], i.e., in presence of an equivalent amount of ethyl bromide.

The so-prepared ethereal solution of pentamethylphenyl magnesium bromide (0.25 mole) was gradually poured into an ethereal solution of 44 g of dimethyl oxalate. After mixing, the ether was replaced by toluene, and the reaction mixture heated on the boiling water bath for a period of 20 hours. Further treatment of the mixture was as in the previous experiments.

The main fraction of 6 g (140-150° at 6 mm) was dissolved in petroleum ether and cooled. The crystals of methyl pentamethyl mandelate were purified by recrystallization from the same solvent. M. pt. 128-129°.

0.1101 g substance: 0.2865 g CO_2; 0.0847 g H_2O. Found %: C 71.00; H 8.61. $C_{14}H_{20}O_3$. Calculated %: C 71.16; H 8.53. 0.1212 g substance: 11.4 ml CH_4 (18°, 758 mm). Found %: OH 6.7. $C_{14}H_{20}O_3$. Calculated %: OH 7.2

The ester has not been described in the literature.

The soda solution was twice washed with ether and then acidified with 10% hydrochloric acid. The resultant yellow crystals of pentamethylphenylglyoxylic acid were purified by recrystallization from toluene. M. pt. 131-132° (yield 20%).

The literature gives a melting point of 122 (from hot alcohol).

0.1136 g substance: 0.2941 g CO_2; 0.0738 g H_2O. Found %: C 70.72; H 7.28. $C_{13}H_{16}O_3$. Calculated %: C 70.80; H 7.32.

SUMMARY

1. A study has been made of the reaction of dimethyl oxalate with equivalent amounts of di-ortho-substituted aryl magnesium bromides. New experimental material has confirmed the validity of the previously proposed mechanism of the reductive reactions which sometimes take place when esters react with organomagnesium compounds.

2. A method is suggested for the preparation of di-ortho-substituted arylglyoxylic acids in a yield of up to 25-30%.

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STERIC HINDRANCE IN ORGANOMAGNESIUM REACTIONS

XIII. PREPARATION OF KETONES BY REACTION OF ACID HALIDES WITH ORGANOMAGNESIUM COMPOUNDS

I. I. Lapkin, N. I. Latosh and E. S. Belov

In one of the previous communications [1] it was pointed out that the existing belief in the impossibility of obtaining ketones by reaction of organomagnesium compounds with halides of monocarboxylic acids only holds good for a relatively small group of low-molecular organomagnesium compounds and acid halides when both components are free from steric hindrance. This is not true of the other groups of these compounds. If in one of the reactants the structure is such as to cause steric hindrance, then the formation of ketones by the reaction in question is quite feasible.

On the basis of the reaction of acetyl and benzoyl chlorides with organomagnesium compounds it was shown that di-ortho-substituted aryl magnesium bromides form only ketones, regardless of the reaction conditions, while mono-ortho-substituted magnesium complexes only yield ketones as the sole product if certain conditions are observed.

The investigations described in the present paper had the objective, firstly, of showing with the help of a large amount of experimental material that the conclusions previously reached were generally valid, and, secondly, of elucidating the influence of the character of the radicals and halides entering into the composition of acid chlorides upon the course of the reaction and the quantitative yield of ketones.

The reactants selected for investigation were, on the one hand, aryl magnesium halides variously substituted in the ortho-position (and thus with varying degrees of steric hindrance) and, on the other hand, chlorides of isovaleric, butyric and isobutyric acids.

Mesityl magnesium bromide reacts with the above chlorides to form isobutyl, propyl and isopropyl mesityl ketones under any reaction conditions (i.e. regardless of the ratio of components, the order of their mixing and the duration of heating).

In contrast to the di-ortho-substituted compounds, the mono-ortho-substituted aryl magnesium halides, particularly o-tolyl magnesium bromide, and also α-naphthyl magnesium bromide whose second ring can be arbitrarily regarded as one ortho-substituent, manifest insufficient hindrance to permit the reaction to be stopped at the stage of ketone formation. Conditions favoring stoppage at the required stage must be created, and then ketones are likewise the sole reaction products. As previously shown [1], such conditions are: Mixing of the reaction components in equimolar amounts, the addition of the Grignard reagent to the cooled ethereal solution of the acid chloride. Under these conditions o-tolyl magnesium bromide and α-naphthyl magnesium bromide react with the chlorides of butyric, valeric and isobutyric acids to form exclusively ketones.

It was impossible to obtain ketones, however, from aryl magnesium halides not substituted in the ortho-position even when the reaction mixture was rather intensively cooled (down to −15°). Formation occurs, side by side with ketones, of products of the second stage of reaction – tertiary alcohols. * Results are presented in Table 1.

The data of Table 1 demonstrate that the yield of ketones is greatly influenced by the nature of the radicals of the halides of monocarboxylic acids. This effect is further illustrated by the data set out in Table 2 in which the percentage yields of ketones are arranged in order of increasing magnitude; the figures in brackets are the yields of dehydration products (tertiary alcohols).

The gradual increase in the ketone yields in the order shown in the table is explained by the fact that the

* In practice not tertiary alcohols but products of their dehydration (unsaturated hydrocarbons) are formed.

TABLE 1

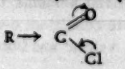
No.	Reaction	Ratio	Ketone	Yield of ketone (%)	Yield of unsat. hydrocarbon (%)
1	Mesityl magnesium bromide + isovaleryl chloride	1:1	Isobutyl mesityl ketone	20	–
2	Mesityl magnesium bromide + isovaleryl chloride	2:1	Isobutyl mesityl ketone	39	–
3	o-Tolyl magnesium bromide + isovaleryl chloride	1:1	Isobutyl o-tolyl ketone	46	–
4	α-Naphthyl magnesium bromide + isovaleryl chloride	1:1	Isobutyl α-naphthyl ketone	52	–
5	p-Tolyl magnesium bromide + isovaleryl chloride	1:1	Isobutyl p-tolyl ketone	39	13
6	Phenyl magnesium bromide + isovaleryl chloride	1:1	Isobutyl phenyl ketone	32	28
7	Mesityl magnesium bromide + butyryl chloride	1:1	Propyl mesityl ketone	18	–
8	Mesityl magnesium bromide + butyryl chloride	2:1	Propyl mesityl ketone	37	–
9	o-Tolyl magnesium bromide + butyryl chloride	1:1	Propyl o-tolyl ketone	42	–
10	α-Naphthyl magnesium bromide + butyryl chloride	1:1	Propyl α-naphthyl ketone	51	–
11	Phenyl magnesium bromide + butyryl chloride	1:1	Propyl phenyl ketone	27	24
12	Mesityl magnesium bromide + isobutyryl chloride	1:1	Isopropyl mesityl ketone	45	–
13	Mesityl magnesium bromide + isobutyryl chloride	2:1	Isopropyl mesityl ketone	55	–
14	o-Tolyl magnesium bromide + isobutyryl chloride	1:1	Isopropyl o-tolyl ketone	53	–
15	α-Naphthyl magnesium bromide + isobutyryl chloride	1:1	Isopropyl α-naphthyl ketone	65	–
16	Phenyl magnesium bromide + isobutyryl chloride	1:1	iso-Propyl phenyl ketone	42	20

TABLE 2

Acid chloride	Aryl magnesium bromide			
	Mesityl	o-Tolyl	α-Naphthyl	Phenyl
Acetyl*	10	30(14)	50(2.5)	19(22)
Butyryl	18	42	51	27(24)
Isovaleryl	20	46	52	32(28)
Isobutyryl	45	53	65	42(20)

* The data for the quantitative yield of ketones due to reaction of acetyl chloride with the aryl magnesium bromides are taken from a preceding paper.

inductive repulsion of electrons by the radicals is intensified in the following order [2,3]: Isopropyl > isobutyl > propyl > methyl. Furthermore an intensification occurs, in the same order, of the statistical effect of conjugation in the acid chlorides in question (A):



(A)

This intensification of effect overlaps that supplementary hindrance which is created by the increased length of the radical chains in the acid chlorides and which is the cause of the gradual rise in ketone yields in the order specified. This rise, however, can only continue to a certain limit. Further increase in length and branching of the chain of the radicals will be accompanied by intensification of the steric hindrance which, of course, results in a fall in the yields of reaction products.

Finally, the reaction course is affected by the nature of the halogen in the halide radical. Since halogens bring about an increase in the statistical effect of conjugation in the order: I > Br > Cl > F, an acid bromide will react with an organomagnesium compound more energetically than a chloride.

Di-ortho-substituted aryl magnesium halides react with acid bromides again with formation exclusively of ketones, but the yield of the latter is considerably higher.

It is more difficult to stop the reaction between mono-ortho-substituted aryl magnesium bromides and acid bromides at the first stage than it is with acid chlorides. Whereas with the latter the preparation of ketones is entirely feasible, with the acid bromides the formation of ketones under the same conditions is accompanied by formation of tertiary alcohol (or, more correctly, of thefr dehydration products in the shape of unsaturated hydrocarbons). Comparative results of reactions of aryl magnesium bromides with acetyl chloride and acetyl bromide are set out in Table 3.

TABLE 3

No.	Reactants	Ratio	Ketone	% yield of ketone	% yield of unsat. hydrocarbons
1	Mesityl magnesium bromide + acetyl chloride	1:1	Methyl mesityl ketone	10	–
2	Mesityl magnesium bromide + acetyl bromide	1:1	Methyl mesityl ketone	26	–
3	Mesityl magnesium bromide + acetyl bromide	2:1	Methyl mesityl ketone	51.5	–
4	o-Tolyl magnesium bromide + acetyl chloride	1:1	Methyl-o-tolyl ketone	30	14
5	o-Tolyl magnesium bromide +acetyl bromide	1:1	Methyl-o-tolyl ketone	20	19
6	α-Naphthyl magnesium bromide + acetyl chloride	1:1	Methyl α-naphthyl ketone	50	2.5
7	α-Naphthyl magnesium bromide + acetyl bromide	1:1	Methyl α-naphthyl ketone	34	10
8	Phenyl magnesium bromide + acetyl chloride	1:1	Methyl phenyl ketone	19	22
9	Phenyl magnesium bromide + acetyl bromide	1:1	Methyl phenyl ketone	17	39

Bromides of monocarboxylic acids can therefore be utilized for preparation of ketones with maintenance of the specified reaction conditions only if the second component is a di-ortho-substituted aryl magnesium halide.

The method of ketone synthesis here developed, based on reaction of acid chlorides with organomagnesium compounds, is highly suitable for the preparation of those carbonyl-containing compounds which are not synthesized by the Gustavson reaction (reaction of hydrocarbons with acid chlorides in presence of anhydrous aluminium chloride) due to the ease of modification of one of the reaction components under the influence of the catalyst. The new synthesis is illustrated by the reaction between camphane carboxylic acid chloride and α-naphthyl magnesium bromide. This reaction yielded bornyl α-naphthyl ketone in an amount corresponding to 60% of the theoretical.

EXPERIMENTAL

The following are the general conditions under which the reaction between organomagnesium compounds and acid halides is performed.

To the acid halide, dissolved in three times the volume of ether and placed in an ice water-cooled flask, is added an ethereal solution of the organomagnesium compound. This order of mixing is suitable both for mono-substituted aryl magnesium bromides and for aryl magnesium bromides not substituted in the ortho-position; however, when mixing the latter class with the ether solution of acid chloride the cooling should be intensified (using snow + salt). In the case of di-ortho-substituted aryl magnesium bromides, the reverse (usual) order of mixing with the acid halides is permissible.

After mixing, the mixture is heated for 6 hours. Although the heating period may be cut down for mono-ortho-substituted and unsubstituted aryl magnesium bromides, the 6-hour period was maintained in all the experiments in order to obtain comparable results. At the end of the heating period addition was made to the reaction mixture of an approximately equal volume of water and heating continued for one hour to permit saponification of the residual acid chloride. Addition was then made of a little dilute acetic acid (sufficient to clarify the ether

solution), the aqueous layer is separated, and the remaining ether layer washed with 10% soda solution and then with water until neutral. The ether solution is dried with anhydrous sodium sulfate and the ether driven off. The reaction products are then distilled in vacuum and analyzed. Results are detailed in Tables 1, 2 and 3.

Synthesis was also effected under the above conditions of bornyl α-naphthyl ketone.

Synthesis of bornyl α-naphthyl ketone. The reactants were 27 g (0.125 mole) naphthyl bromide, 4 g magnesium and 24 g (0.125 mole) camphane carboxylic acid chloride. The main fraction (210-220° at 7 mm) amounted to 28.0 g. The residue in the flask weighed 1 g. A second distillation of the main fraction gave 24.0 g boiling at 218-219° (7 mm) or 66 % of theory. The substance rapidly crystallized and after 3 recrystallizations from petroleum ether had the constant m. pt. of 109-110° (bornyl α-naphthyl ketone). This ketone has not been described in the literature.

0.1564 g substance: 0.4939 g CO_2; 0.1250 g H_2O. Found %: C 86.17; H 8.30. $C_{21}H_{24}O$. Calculated %: C 86.26; H 8.26.

To one part of the ketone dissolved in glacial acetic acid was added a slight excess of phenylhydrazine. After standing for 10 hours the crystalline phenylhydrazone of bornyl α-naphthyl ketone had separated, M. pt. 128° from toluene).

0.1244 g substance: 7.8 ml N_2 (20°, 760 mm). Found %: N 7.33. $C_{27}H_{30}N_2$. Calculated %: N 7.31.

Another portion of the ketone was reduced (Clemenson reaction) to a hydrocarbon – bornyl α-naphthyl methane. B. pt. 239° (14 mm), m. pt. 104° (from petroleum ether).

0.1952 g substance: 0.6474 g CO_2; 0.1652 g H_2O. Found %: C 90.51; H 9.47. $C_{21}H_{28}$. Calculated %: C 90.59; H 9.41.

SUMMARY

1. By means of a much larger amount of experimental material, confirmation was obtained of previous conclusions regarding the possibility of preparing ketones as the sole products of reaction of ortho-substituted aryl magnesium halides with monocarboxylic acid halides.

2. It was established that the quantitative yield of ketones is markedly affected by the character of the radical and by the character of the halogen entering into the composition of the acid chloride.

3. It was also shown that the method of synthesis which was developed is very suitable for the preparation of those carbonyl-containing compounds which cannot be synthesized by the Gustavson reduction due to the ease of modification of one of the reactants in presence of the catalyst.

4. Three compounds not known in the literature are described: Bornyl α-naphthyl methane, bornyl α-naphthyl ketone and its phenylhydrazone.

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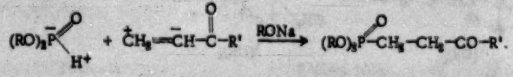
* See Consultants Bureau translation, p. 677.

ADDITION OF DIALKYL PHOSPHOROUS ACIDS TO UNSATURATED COMPOUNDS

VII. ADDITION OF DIALKYL PHOSPHOROUS ACIDS TO α,β-UNSATURATED KETONES OF THE ALIPHATIC SERIES

A. N. Pudovik

In a series of previous papers we have shown that in presence of alkali metal alcoholates the dialkyl phosphorous acids add on extremely energetically and rapidly to α,β-unsaturated ketones with formation of esters of β-ketophosphonic acids. Yields of 60-75 % were obtained of the products of addition of dialkyl phosphorous acids to β,β-dimethyldivinyl ketone, ethylideneacetone, benzylidene acetone and furfurylidene acetone [1]. Using β,β-dimethyldivinyl ketone as an example, it was shown that when using equimolar amounts of acid and ketone the addition takes place only at the unsubstituted vinyl group, and, in accordance with the general principles of electronic theory, it proceeds in such a manner that the negatively polarized phosphonium group adds on to the positively polarized β-carbon atom of the vinyl group:



A similar order of addition, as we previously demonstrated, is observed also in all other cases of addition of dialkyl phosphorous acids to α,β-unsaturated electrophilic reagents: Unsaturated nitriles [2], aldehydes and esters of carboxylic acids [3].

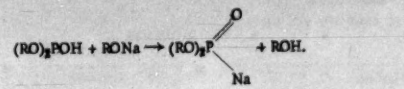
In a study of the addition of dialkyl phosphorous acids to β-substituted vinyl ketones it was also noted that the presence of substituted groups, especially phenyl, reduce in large measure the velocity of the addition reaction in comparison with the unsubstituted vinyl group of dimethyldivinyl ketone. This observation may be explained by the reduction of the electrophilic character of β-carbon atom by the presence of substituents which possibly create certain steric hindrances in addition.

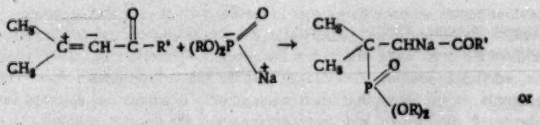
In continuing and developing the investigation started by us, it appeared of interest to study the addition of dialkyl phosphorous acids to monovinyl ketones with a still larger number of substituents on the vinyl group and to elucidate the influence of their nature, distribution and number on the speed and order of the addition. From this aspect we instituted experiments on the addition of dialkyl phosphorous acids to mesityl oxide, β,β-dimethylvinyl-β'-methoxyethyl ketone, α,β-dimethylvinyl methyl ketone , and α-methylvinyl-γ-methoxypropyl ketone.

In the first instance we performed experiments with mesityl oxide and β,β-dimethylvinyl-β'-methoxyethyl ketone, each with two methyl groups at the β-carbon atom. In order to avoid radical exchange between the molecules of dialkyl phosphorous acids and the alcoholates used as catalysts, and in order also to ensure maximum purity of the resultant addition products, the alcoholates were prepared from alcohols with the same radicals as entered into the composition of the dialkyl phosphorous acids.

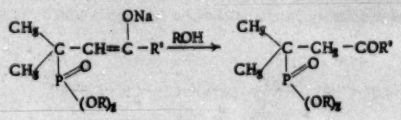
It may be suggested that the presence of two methyl groups on the β-carbon atom of the vinyl group may so reduce its electrophilic character and modify its spatial characteristics that more favorable conditions will be created for addition of dialkyl phosphorous acids not at the double bond but at the carbonyl group. In fact, it was observed that addition in the case of both of the ketones proceeds much less energetically in comparison with ketones containing an unsubstituted vinyl group or one substituent at the β-carbon atom, and requires for its completion rather large amounts of a saturated alcoholic solution of the alcoholate (up to several milliliters). With mesityl oxide the yields of addition products were of the order of 68-78%; with β,β-dimethyl-β'-methoxyethyl ketone they were very low; the main bulk of reaction mixture was converted during distillation into a nearly solid vitreous mass; in the pure form the only addition product isolated was diethyl phosphorous acid. For the purpose of determining the structure of the prepared addition products we first chose Tserevitinov's method as being simpler and more convenient (determination of the presence of hydroxyl groups). It was found that at room temperature the addition products

react with methyl magnesium iodide only very slowly and incompletely; on heating, the reaction proceeds rapidly and the hydroxyl group can be determined with little error. On this basis we arrived at the preliminary conclusion that the prepared addition products can be regarded as unsaturated hydroxyphosphonic esters [4]. A more detailed study of the properties of the products, however, did not confirm this assumption. It was found that these products do not add on bromine and were not oxidized by potassium permanganate; on acting with phenylhydrazine upon the products of addition of diethyl phosphorous acid to mesityl oxide, a phenylhydrazone was obtained in 69% yield. These results led us to the conclusion that the addition products are not unsaturated α-hydroxyphosphonic esters but esters of β-ketophosphonic acids. The reaction proceeds according to the scheme:





or



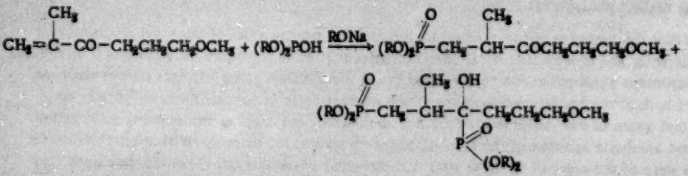
where R' = CH_3 or $CH_2CH_2OCH_3$

The constants, yields, and analytical data are set forth in Table 1. *

The results of quantitative determinations of hydroxyl groups** in the prepared esters of β-ketophosphonic acids by the Tserevitinov method are undoubtedly due to enolization of the carbonyl groups which proceeds slowly at room temperature but rapidly on heating.

We also obtained analogous results when investigating the addition of dialkylphosphorous acids to α,β-dimethylvinyl ketone. The addition products likewise do not add on bromine and are not oxidized by permanganate. The phenylhydrazone prepared from the ketone-diethyl phosphorous acid addition product was a very viscous oil which decomposed with evolution of a large amount of very volatile substances when an attempt was made to distill it in a vacuum (1 mm). The constants and yields of the prepared 3-methyl-4-dialkylphosphopentanones-2 are presented in Table 2.

Slightly different results were obtained in the addition reaction of dialkyl phosphorous acids and α-methyl-vinyl-γ-methoxypropyl ketone synthesized by the method of Nazarov and Zaretskaya [5]. Addition to this ketone of dimethyl phosphorous acid and diethyl phosphorous acid resulted in each case in the formation of two products: a low-boiling product of addition of one molecule of dialkyl phosphorous acid, and a high-boiling product of addition of two molecules of dialkyl phosphorous acid. In the second case the addition clearly proceeds both at the double bond and at the carbonyl group; part of the unreacted unsaturated ketone is recovered unchanged on distillation:



Accurate determination of the hydroxyl groups in the prepared esters of hydroxydiphosphinic acids proved impossible due to their poor solubility in the dibutyl and diisoamyl ethers used as solvents.

* All the experiments were performed with heating of the reaction mixture at 90-95° for 30-60 minutes with occasional stirring.

** Hydroxyl group determinations were made at 90-95°.

TABLE 1

No.	Formula	Boiling point	n_D^{20}	d_4^{20}	Phosphorus content (%) Found	Phosphorus content (%) Calcd.	Hydroxyl group content (%) Found	Hydroxyl group content (%) Calcd.	Yield (%)
1	$(CH_3O)_2P(O)-C(CH_3)_2-CH_2COCH_3$	136° (12 mm)	1.4457	1.1163	14.9	15.3	–	–	70.3
2	$(C_2H_5O)_2P(O)-C(CH_3)_2CH_2COCH_3$	138 (11 mm)	1.4400	1.0675	13.4	13.1	7.7	7.2	78.6
3	$(iso\text{-}C_4H_9O)_2P(O)-C(CH_3)_2CH_2COCH_3$	162-163 (12 mm)	1.4409	1.0029	10.8	10.6	6.2	5.8	68.7
4	$(n\text{-}C_4H_9O)_2P(O)-C(CH_3)_2CH_2COCH_3$	171-172 (13 mm)	1.4440	1.0084	10.5	10.6	–	–	77.2
5	$(C_2H_5O)_2P(O)-C(CH_3)_2CH_2-CO-CH_2CH_2OCH_3$	164-168 (10 mm)	1.4500	1.1129	13.5	13.1	6.7	6.1	12

TABLE 2

No.	Formula	Boiling point	n_D^{20}	d_4^{20}	Hydroxyl group content (%) Found	Hydroxyl group content (%) Calcd.	Yield (%)
1	$(CH_3O)_2P(O)-CH(CH_3)-CH(CH_3)-CO-CH_3$	136-137° (11 mm)	1.4475	1.1159	8.1	8.1	50.4
2	$(C_2H_5O)_2P(O)-CH(CH_3)-CH(CH_3)-CO-CH_3$	158° (20 mm)	1.4390	1.0442	7.7	7.2	66.3

As we pointed out in a previous paper [2] the addition of a second molecule of dialkyl phosphorous acids to the carbonyl groups proceeds also with all the other ketophosphonic acids which we had previously prepared, but only after completion of the addition of the first molecule of dialkyl phosphorous acid at the double bond of the unsaturated ketone.

Saponification of the esters of β-ketophosphonic acids in the presence of dilute hydrochloric acid yielded the β-ketophosphonic acids themselves in the form of viscous, straw-colored liquids. Also prepared and analyzed was the acid barium salt of 4-methyl-4-phosphopentanone-2, a white powder.

EXPERIMENTAL

Addition of dialkyl phosphorous acids to mesityl oxide and β,β-dimethyl-β'-methoxy-ethyl ketone. The addition was performed by the following general method: to a mixture of equimolar amounts of ketone and dialkyl phosphorous acid was added dropwise an alcoholic solution of sodium alcoholate. The alcoholic solution of sodium alcoholate was prepared with an alcohol containing the same radical as that entering into the composition of the dialkyl phosphorous acid. Increasing molecular weight of the dialkyl phosphorous acids was accompanied by a marked fall in the velocity of the addition reaction. After addition of the amount of alcoholate required for completion of the addition reaction, the reaction mixture was allowed to stand for 20-30 minutes and, after cooling, it was then distilled in vacuum from a small Arbuzov flask. The constants, yields, and analyses of the obtained products are set forth in Table 1.

Investigation of the properties of 4-methyl-4-diethylphosphotentanone-2. 1. Action of bromine. The determination was performed by the McIlhiney method in chloroform solution. Estimation was made of the bromine consumed on addition and substitution. The series of experiments led to the conclusion that substantially no addition occurs, when the sample is dissolved in bromine-in-chloroform, during the first 10-50 minutes and that substitution takes place but only to an insignificant degree. Beginning, however, at a certain instant, calculated at 1½-2

hours from the start of the experiment, the bromine solution is almost instantaneously decolorized, signalizing a rapid substitution reaction. Supplementary amounts of bromine added to the reaction mixture after this moment were also very rapidly consumed by substitution.

2. Oxidation by potassium permanganate. 4.8 g of product was dissolved in 200 ml of water, followed by about 1 g of potassium permanganate (one-seventh of the theoretically required quantity). Even after standing for 5 days at room temperature, there was no decolorization or formation of manganese dioxide precipitate.

3. Preparation of the phenylhydrazone. Into a porcelain beaker were weighed 5 g ketone and 3 g phenylhydrazine, after which 10 ml absolute ethyl alcohol was run in. The solution was kept in a desiccator for 3 days at room temperature and then heated on the boiling water bath for 4 hours. No crystallization was observed even after cooling followed by prolonged standing at 0°. Vacuum distillation of the reaction mixture yielded 4.7 g of the phenylhydrazone of 4-methyl-4-diethylphosphopentanone-2 with b.p. 202-203° (4 mm) in the form of a very viscous, oily liquid with a light-brown color.

0.1624 g substance: 32.3 ml NaOH (T 0.017841). Found %: P 9.8. $C_{18}H_{31}O_3PN_2$. Calculated %: P 9.5.

4. Saponification with hydrochloric acid. 3.6 g product with 60 ml dilute hydrochloric acid (1:1) were heated in a sealed tube at 130-140° for 9 hours. A total of 1.6 g ethyl chloride was formed (the theoretical requirement is 1.8 g). Following evaporation of the reaction mixture for many hours with periodic addition of distilled water, the whole of the hydrochloric acid was driven off. Evaporation of the aqueous solution yielded the ketophosphonic acid in the form of a straw-colored viscous liquid. Even after prolonged standing the acid did not crystallize. The barium salt (a white powder) was prepared from it.

0.9344 g substance: 0.4505 g $BaSO_4$. Found %: Ba 28.3. $C_{18}H_{36}O_8P_2Ba$. Calculated %: BA 27.7.

Addition of dimethyl phosphorous acid to α,β-dimethylvinylmethyl ketone. To a mixture of 9.8 g ketone and 11 g dimethyl phosphorous acid was added dropwise a saturated solution of sodium methylate in methyl alcohol. The reaction only started after 10-15 drops of methylate had been added, and proceeded with considerable heat evolution with continued addition. Distillation of the reaction mixture gave 14.1 g of 3-methyl-4-dimethylphosphopentanone-2:

B.p. 136-137° (11 mm); n_D^{20} 1.4475; d_4^{20} 1.1159.

0.1686 g, 0.1364 g substance: 50.7 ml, 41.4 ml NaOH (T 0.017841).
Found %: P 14.9, 15.0. $C_9H_{19}O_4P$. Calculated %: P 14.9.

Examination of the product showed that it did not add on bromine (only substitution occurred) and was not oxidized by permanganate. With phenylhydrazine it gave a phenylhydrazone in the form of a very viscous, brown oil. An attempt to fractionate the phenylhydrazone in vacuum (1 mm) was accompanied by violent decomposition with evolution of a large quantity of white fumes and of low-boiling products which condensed in the condenser. Saponification of the phosphonic ester gave the ketophosphonic acid in the form of a thick, straw-colored liquid.

Addition of diethyl phosphorous acid to α,β-dimethylvinyl methyl ketone. To a mixture of 4 g ketone and 5.5 g diethylphosphorous acid was added dropwise a saturated solution of sodium ethylate in ethyl alcohol. After termination of the reaction and cooling, the mixture was fractionated from a small Arbuzov flask, giving 6.3 g of 3-methyl-4-diethylphosphopentanone-2.

B.p. 158° (20 mm); n_D^{20} 1.4390; d_4^{20} 1.0442.

0.1626 g substance: 41.7 ml NaOH (T 0.017841). Found %: P 12.7. $C_{13}H_{27}O_4P$. Calculated %: P 13.1.

Addition of dimethyl phosphorous acid to α-methylvinyl-γ-methoxypropyl ketone. 11 g of α-methylvinyl-γ-methoxypropyl ketone (b.p. 60-62° (10 mm); n_D^{20} 1.4430) was reacted with 14.2 g dimethyl phosphorous acid, using sodium methylate solution as catalyst. Addition of the methylate to the reaction mixture led to considerable heating. After the reaction had been cooled and allowed to stand at room temperature for an hour, it was distilled in vacuum to give two substances: a) 1-Dimethylphosphone-2-methyl-6-methoxyhexanone-3 (2.1 g):

B.p. 161-164° (11 mm) n_D^{20} 1.4656; d_4^{20} 1.1098.

0.1470 g, 0.2018 g substance: 38.0 ml, 52.1 ml NaOH (T 0.01768).
Found %: P 12.6, 12.6. $C_{10}H_{21}O_5P$. Calculated %: P 12.3.

b) 1,3-Di-(dimethylphosphone)-2-methyl-6-methoxyhexanol-3 (5.1 g):

B.p. 236-238° (16 mm); n_D^{20} 1.4840; d_4^{20} 1.2055.

0.1298 g, 0.1178 g substance: 45.4 ml; 41.1 ml NaOH (T 0.01768). Found %: P 17.1, 17.1. $C_{18}H_{32}O_6P_2$. Calculated %: P 17.1.

Addition of diethyl phosphorous acid to α-methylvinyl-γ-methoxypropyl ketone. To a mixture of 12 g of the ketone and 11.6 g of the acid was added, dropwise, a saturated solution of sodium ethylate in ethyl alcohol. The following substances were isolated after the reaction and distillation:

a) 1-Diethylphosphone-2-methyl-6-methoxyhexanone-3 (4.7 g):

B.p. 167-168° (12 mm); n_D^{20} 1.4620; d_4^{20} 1.0590.

Found %: P 10.98, 10.96. $C_{12}H_{25}O_5P$. Calculated %: P 11.06.

b) 1,3-Di-(diethylphosphone)-2-methyl-6-methoxyhexanol-3 (5.3 g):

B.p. 226-227° (12 mm); n_D^{20} 1.4769; d_4^{20} 1.1214.

0.1638 g substance: 50.2 ml NaOH (T 0.01768). Found %: P 15.0 $C_{18}H_{39}O_8P_3$. Calculated %: P 14.8.

SUMMARY

1. A study was made of the addition of dialkyl phosphorous acids to mesityl oxide, β,β-dimethylvinyl-β'-methoxyethyl ketone, α,β-dimethylvinyl methyl ketone and α-methylvinyl-γ-methoxypropyl ketone. In all cases addition takes place at the double bond with formation of the corresponding esters of ketophosphonic acids. In the case of α-methylvinyl-γ-methoxypropyl ketone, products of addition of two molecules of the dialkyl phosphorous acids are also obtained: addition proceeds both at the double bond and at the carbonyl group.

2. The presence of two methyl groups at the α- and β-carbon atoms, and particularly at the β-carbon atom, of the vinyl group of the unsaturated ketones sharply reduces the speed of addition of dialkyl phosphorous acids to them.

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ALLYL REARRANGEMENTS

XVI. FORMATION OF ACETATES AND ALCOHOLS FROM BUTOXYCHLOROPENTENES

A. N. Pudovik and V. I. Nikitina

In a series of previous papers we have described the saponification reactions of isomeric methoxychloropentenes [1] and dichlorobutenes [2] and the preparation from them of acetates by the action of sodium acetate. It was shown that two mechanisms are involved: Bimolecular nucleophilic substitution leading to products without rearrangement; and a monomolecular mechanism yielding carbonium ions and leading to identical mixtures of products of both of the isomeric chlorides. Primary haloallyl isomers react predominantly according to the bimolecular mechanism in the reactions of saponification and of ester formation, while secondary compounds react according to the monomolecular mechanism.

The purpose of the present investigation was the further study of the saponification reactions and of the formation of acetates from haloallyl compounds with reference to the reactions of the primary and secondary butoxychloropentenes, and the elucidation of the effect of the $C_4H_9OCH_2CH_2$ radical in them upon the ratio of the substitution reactions. On acting with potassium acetate upon 1-butoxy-5-chloro-3-pentene in acetic acid solution, we obtained a mixture of acetates consisting of 93% of 1-butoxy-3-penten-5-yl acetate and 7% of 1-butoxy-4-penten-3-yl acetate. The total yield of acetates was 81%. An experiment under analogous conditions with 1-butoxy-3-chloropentene-4 gave a mixture of 59% of 1-butoxy-3-penten-5-yl acetate and 41% of 1-butoxy-4-penten-3-yl acetate. The acetates are stable and show little tendency to change either under thermal isomerization conditions (100°) or on heating in acetic acid solution, i.e. under conditions similar to those used in their preparation.

When our paper was completed a paper appeared by Emerson, Dubel and Longley [3] which describes the preparation of a series of alkoxychloropentenes, a large number of which had previously been prepared and described by us [4], likewise the reactions of some of them. They gave details, in particular, of the reaction of 1-butoxy-5-chloro-3-pentene with sodium acetate in acetic acid solution, but they only succeeded in isolating one product — 1-butoxy-3-penten-5-yl acetate in 77% yield, whose constants were identical with those of our own preparation. In general they did not study the reaction with the secondary chloride.

The saponification of both of the isomeric acetates of butoxypentenols, under our conditions, proceeds without isomerization, thus providing an additional proof of the fact that saponification of esters of alcohols of the allyl type proceeds without rupture of the alcoholic carbon-oxygen bond, and consequently, without formation of the carbonium ion. We effected the saponification of the isomeric butoxychloropentenes with aqueous sodium carbonate. Saponification of 1-butoxy-5-chloro-3-pentene gave a mixture of alcohols consisting of 79% 1-butoxy-3-penten-5-ol and 20.3% 1-butoxy-4-penten-3-ol, while the mixture obtained from 1-butoxy-3-chloro-4-pentene comprised 56.8% 1-butoxy-3-penten-5-ol and 43% 1-butoxy-4-penten-3-ol. The results in the present investigation are very similar to those in the preceding papers [1,2]. In analogy with the earlier investigations, we may conclude that saponification of secondary butoxychloropentene and its reaction with alkali metal acetates proceed mainly according to a monomolecular mechanism, while the primary compound reacts according to a mixed mono- and bimolecular mechanism. On the basis of the present results we may also conclude that substitution of the radical $CH_3OCH_2CH_2$ for $C_4H_9OCH_2CH_2$ in the haloallyl system has very little influence upon the relative extents of the substitution reactions of the halide with the hydroxyl and acetate groups, which proceed according to the bimolecular and monomolecular mechanisms.

EXPERIMENTAL

Action of potassium acetate on 1-butoxy-5-chloro-3-pentene in acetic acid solution. 39.5 g 1-butoxy-5-chloro-3-pentene, 23 g glacial acetic acid and 30 g calcined potassium acetate were heated for 27 hours at a bath temperature of 140-150°. After cooling, the reaction mixture was treated with water and then with soda solution prior to extraction with ether. The ether extract was dried with calcium chloride, the ether

driven off, and the residue distilled in vacuum, using a spiral column. 2.5 g 1-butoxyl-4-penten-3-yl acetate was obtained.

B.p. 99-100° at 9 mm; n_D^{20} 1.4298; d_4^{20} 0.9240; MR_D 55.89; calculated 55.71.

0.1204 g substance: 0.2908 g CO_2; 0.1048 g H_2O. Found %: C 65.91; H 10.2. $C_{11}H_{20}O_2$. Calculated %: C 66.00; H 10.00.

There was also obtained 34 g 1-butoxy-3-penten-5-yl acetate:

B.p. 116-117° at 9 mm; n_D^{20} 1.4390; d_4^{20} 0.9399; MR_D 55.97; calculated 55.71.

0.0975 g substance: 0.2353 g CO_2; 0.0856 g H_2O. Found %: C 65.86; H 9.82. $C_{11}H_{20}O_2$. Calculated %: C 66.00; H 10.00.

Addition of bromine to 1-butoxy-3-penten-5-yl acetate gave the dibromide:

B.p. 173-175° at 17 mm; n_D^{20} 1.4840; d_4^{20} 1.4267; MR_D 72.10; calculated 71.75.

0.1298 g substance: 0.1345 g AgBr. Found %: Br 44.06. $C_{11}H_{20}O_2Br_2$. Calculated %: Br 44.38.

Action of potassium acetate on 1-butoxy-3-chloro-4-pentene in acetic acid solution. 39.5 g 1-butoxy-3-chloro-4-pentene, 23 g glacial acetic acid and 30 g powdered anhydrous potassium acetate were heated at a bath temperature of 130-140° for 46 hours. Treatment of the reaction mixture was as above. Distillation of the products yielded 10.4 g 1-butoxy-4-penten-4-yl-acetate:

B.p. 98.5-99° at 8.5 mm; n_D^{20} 1.4300; d_4^{20} 0.9240,

and 14.9 g 1-butoxy-3-penten-5-yl acetate:

B.p. 115-116° at 8.5 mm; n_D^{20} 1.4390; d_4^{20} 0.9399.

The dibromide was obtained by reacting bromine with 1-butoxy-4-penten-3-yl acetate:

B.p. 162-164° at 12 mm; n_D^{20} 1.4810; d_4^{20} 1.4230; MR_D 71.92; calculated 71.75.

0.1134 g substance: 0.1181 g AgBr. Found %: Br 44.28. $C_{11}H_{20}O_2Br_2$. Calculated %: Br 44.38.

Experiments on determination of the stability of the isomeric pentenyl acetates.

Experiment 1. Glass ampoules containing respectively 1 g 1-butoxy-4-penten-3-yl acetate (n_D^{20} 1.4300) and 1 g 1-butoxy-3-penten-5-yl acetate (n_D^{20} 1.4390) were heated for 33 hours at 100°. No change in the refractive indices of the acetates was observed.

Experiment 2. Mixtures comprising 6 g acetic acid and 10 g, respectively, of 1-butoxy-4-penten-3-yl acetate and 1-butoxy-3-penten-5-yl acetate were heated for 33 hours at the temperature of the boiling water bath. Both isomers remained unchanged after the heating.

Saponification of 1-butoxy-3-penten-5-yl acetate. 6 g KOH was dissolved in 54 ml 96% alcohol, and to the solution was added 19.5 g 1-butoxy-3-penten-5-yl acetate. The mixture was heated on the water bath under a reflux condenser with mechanical stirring for 6 hours. After the alcohol had been driven off, the residue was treated with soda and extracted with ether. Fractionation of the residue after removal of the ether gave 10.6 g 1-butoxy-3-penten-5-ol:

B.p. 113-114° at 9 mm; n_D^{20} 1.4508; d_4^{20} 0.9115; MR_D 46.65; calculated 46.46.

0.1148 g substance: 0.2873 g CO_2; 0.0929 g H_2O. Found %: C 68.30; H 11.40; $C_9H_{18}O_2$. Calculated %: C 68.35; H 11.39.

Treatment of this alcohol with bromine gave the dibromide:

B.p. 157-158° at 7 mm; n_D^{20} 1.5071; d_4^{20} 1.5161; MR_D 62.35; calculated 62.38.

0.1254 g substance: 0.1480 g AgBr. Found %: Br 50.18. $C_9H_{18}O_2Br_2$. Calculated %: Br 50.25.

Saponification of 1-butoxy-4-penten-3-yl acetate. 3.6 g KOH was dissolved in 33 ml 96% alcohol, and to the solution was added 12 g 1-butoxy-4-penten-3-yl acetate. The mixture was heated on the water bath for 8 hours. The reaction mixture was worked up and distilled to give 7.2 g 1-butoxy-4-penten-3-ol:

B.p. 91-92° at 9 mm; n_D^{20} 1.4404; d_4^{20} 0.8995; MR_D 46.34; calculated 46.46.

0.1113 g substance: 0.2781 g CO_2; 0.1116 g H_2O. Found %: C 68.19; H 11.22. $C_5H_{12}O_2$. Calculated %: C 68.35; H 11.39.

Treatment with bromine gave the dibromide:

B.p. 154-155° at 6 mm; n_D^{20} 1.5030; d_4^{20} 1.5124; MR_D 62.08; calculated 62.38.

0.1163 g substance: 0.1368 g AgBr. Found %: Br 50.01. $C_5H_{12}O_2Br_2$. Calculated %: Br 50.26.

SUMMARY

1. A study was made of the reaction of the isomeric butoxychloropentenes with potassium acetate and of their saponification with aqueous sodium carbonate solution.

2. It was shown that the hydrolysis and formation of acetates from primary butoxychloropentene take place according to a mixed mono- and bimolecular mechanism with the latter predominating. Similar reactions with secondary butoxychloropentene proceed mainly according to a monomolecular mechanism.

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*See Consultants Bureau translation, p. 1173.

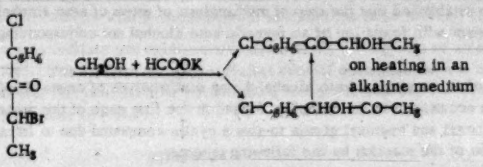
** See Consultants Bureau translation, p. 241.

MOLECULAR REARRANGEMENTS OF α-KETO ALCOHOLS

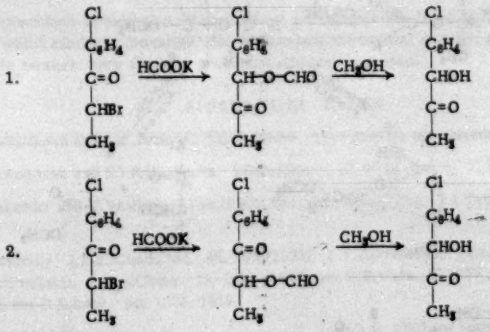
XI. MOLECULAR REARRANGEMENTS DURING METHANOLYSIS OF ESTERS OF α-KETO ALCOHOLS

T. I. Temnikova and E. I. Kulachkova-Kmito

In previous investigations [1,2] it was shown that in the synthesis of some α-keto alcohols by the Klint method, the normal products of reaction are accompanied, as anticipated, by isomeric α-keto alcohols. The formation of a mixture of isomeric keto alcohols in this reaction was noted in a series of papers [3], but in all the previously studied examples the isomeric keto alcohols – the abnormal reaction products – were more stable, and their formation was explained by the isomerization of the primary normal reaction products. In the cases investigated by us the isomeric keto alcohols proved to be less stable and when heated under alkaline conditions they were transformed into the α-keto alcohols which are the normal reaction products:



In explanation of this phenomenon we put forward two possible mechanisms of the formation of the anomalous keto alcohol:



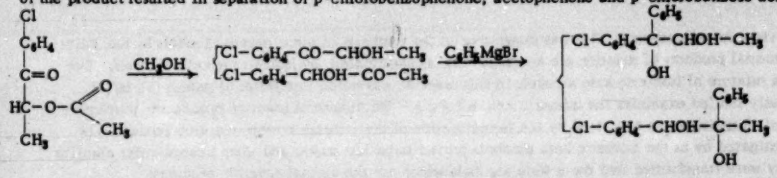
According to the first variant, molecular rearrangement takes place during the formation of the ester of the keto alcohol from the bromo ketone; this type of rearrangement has been described in the literature [4].

In the second case it is proposed that rearrangement occurs during the stage of methanolysis of the ester. Molecular rearrangements during methanolysis of esters of keto alcohols have not been described in the literature. On the basis of theoretical considerations we have considered the second variant to be more probable. The present investigation had the objective of throwing more light upon this stage.

Attempts to elucidate the process of separation of the formate of the keto alcohol and obtain evidence of its structure did not succeed. When the bromo ketone was reacted with potassium formate in a medium of 98% formic acid, the resultant product (distilled in vacuum) contained a considerable amount of the keto alcohol. Formation of the keto alcohol could proceed both through partial hydrolysis with water present in the reaction mixture and through decomposition of the formate during the distillation.

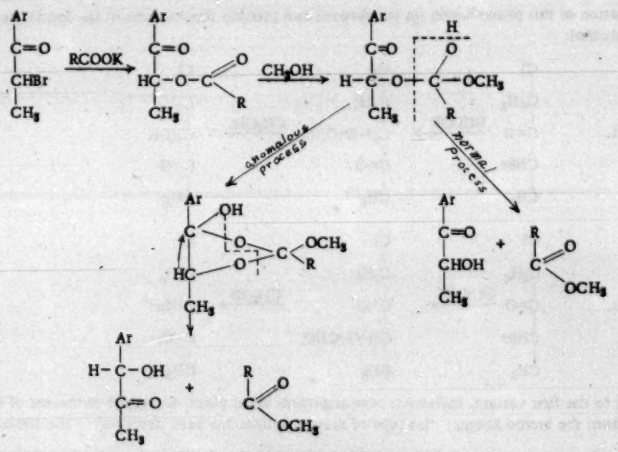
It was therefore impossible to obtain direct evidence of the rearrangement mechanism. In view of the failure to prepare the pure formate of the keto alcohol, experiments were performed to establish the possibility of extending the reaction to other esters or of effecting the methanolysis of the other esters of α-keto alcohols. In the present investigation we have studied the methanolysis of methyl-p-chlorobenzoyl carbinol acetate.

The acetate was prepared by the action of potassium acetate upon α-bromoethyl-p-chlorophenyl ketone and, as was shown in the previous communication, did not contain the isomeric acetate [2]. Heating of the ester on the boiling water bath with methyl alcohol for 20 hours in presence of sodium formate gave a mixture of keto alcohols in approximately the same ratio as was obtained in the methanolysis of the formic ester. Evidence of the presence of a mixture of keto alcohols was obtained by their conversion into glycols with the help of C_6H_5MgBr. Oxidation of the product resulted in separation of p-chlorobenzophenone, acetophenone and p-chlorobenzoic acid.



It has thus been established that the step of methanolysis of esters of keto alcohols may be complicated by a molecular rearrangement with formation of an isomeric keto alcohol not corresponding in structure to the initial bromo ketone.

The formation of an isomeric α-keto alcohol during methanolysis of esters of α-keto alcohols can be accounted for only by the occurrence in the complex, formed in the first stage of the process, of supplementary interaction between the carbonyl and hydroxyl groups to give a cyclic compound due to intramolecular addition. We may represent the course of the reaction by the following scheme:



EXPERIMENTAL

1. Action of sodium formate on α-bromoethyl-p-chlorophenyl ketone. 42 g α-bromoketone, 60 g anhydrous sodium formate and 100 ml formic acid (98%; d 1.2220) were heated for 30 hours at 100°. At the end of the reaction the formic acid was distilled off in vacuum and the residue distilled over at 134-137° (5 mm). Yield 6.2 g.

d_4^{20} 1.2457; n_D^{20} 1.5459; number of OH groups: 0.52, 0.52, 0.41.

2. Methanolysis of methyl-p-chlorobenzoyl carbinol acetate by methyl alcohol. Use was made of the ester prepared by the earlier described method [2]. It had b.p. 127-130° (1.5 mm) n_D^{16} 1.5332. 13 g of ester dissolved in 35 ml absolute methyl alcohol was heated on the boiling water bath with 10 g anhydrous sodium formate. At the conclusion of the reaction, the alcohol was distilled off in vacuum and the residue washed with water and extracted

with ether. The ether extract was dried with magnesium sulfate, the ether driven off, and the residue distilled in vacuum.

B.p. 112-114° at 1.5 mm; d_4^{16} 1.255; d_4^{20} 1.245; n_D^{16} 1.553; n_D^{20} 1.5498; MR_D found 47.04, calc. 46.564.

Yield 6 g of keto alcohol or 60% of theoretical. From 0.6 g was obtained 0.62 g semicarbazone with b.p. 176-178°.

Action of C_6H_5MgBr on the reaction product. To the C_6H_5MgBr obtained from 3.2 g Mg and 21 g bromobenzene while cooling with ice was added 5 g of reaction product. After the usual treatment [2] followed by removal of the ether, the material was dissolved in a large amount of ligroin from which spherical crystals separated. M.p. 88-90°. Yield 1.8 g.

0.0913 g substance: 0.2302 g CO_2; 0.0481 g H_2O. 0.0404 g substance: 0.1020 g CO_2; 0.0202 g H_2O. Found %: C 68.76, 68.85; H 5.89, 5.59. $C_{15}H_{13}O_2Cl$. Calculated %: C 68.58; H 5.71.

Oxidation of the reaction product. To 1.3 g substance was added 10 g lead tetraacetate in 20 ml glacial acetic acid and oxidation was performed at 55-65°. Further treatment was as before [2]. Steam-distillation yielded first an oil with the odor of acetophenone and then a solid which solidified in the condenser and melted, after drying, at 68-72°. A mixture with an authentic specimen of p-chlorobenzophenone (m.p. 72-74°) melted at 70-73°. The residue from the steam distillation was extracted with ether to give a crystalline, readily distillable compound with m.p. 233-235°. A mixture with p-chlorobenzoic acid had the same melting point.

The first part of the steam-distillate was oxidized with silver oxide for removal of aldehydes from the neutral oil and again steam-distilled. The distilled oil with a distinct odor of acetophenone was converted into the semicarbazone which, after several recrystallizations from alcohol, melted at 198-201°. A mixture with acetophenone semicarbazone also melted at 197-200°.

SUMMARY

1. Heating of methyl-p-chlorobenzoyl carbinol acetate with methyl alcohol in presence of sodium formate leads to methanolysis of the ester.

2. The methanolysis of methyl-p-chlorobenzoyl carbinol acetate is shown to be complicated by a molecular rearrangement which results in formation, side by side with the normal reaction product (methyl-p-chlorobenzoyl carbinol), of the isomeric keto alcohol — p-chlorophenylacetyl carbinol.

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CHEMICAL REACTIONS AT EXTREMELY HIGH PRESSURES

I. REACTION OF BENZENE WITH ANHYDROUS ALUMINUM CHLORIDE

M.G.Gonikberg and A.E.Gavrilova

Several authors have studied the action of anhydrous aluminum chloride on benzene: G.Gustavson [1] (1878 and later), Friedel and Crafts [2] (1882-1885), and others (see the survey of these investigations [3]). The reaction gives a complex mixture of hydrocarbons from which were isolated phenylcyclohexane, o-diphenylcyclohexane and 3-phenyl-1-methylcyclopentane. There are also indications of the presence in the reaction products of diphenyl, ethylbenzene, toluene and naphthalene (at higher temperatures). The yield of products was found to be most insignificant in spite of the experiments being prolonged for several weeks. For instance, in the experiments of Wertyporoch and Sagel [4] the total yield of products of reactions of benzene with aluminum chloride at 30° for 12 weeks was 8% of the weight of benzene.

No previous study has been reported on the effect of pressure on the reaction.

EXPERIMENTAL*

We performed experiments with anhydrous $AlCl_3$ and dry benzene (thiophene-free) taken in molar ratios of 0.8:1, using a stainless steel reactor at pressures up to 3300 atm. The reactor was fitted with a valve and pressure gage; heating was by an electric furnace covering the reactor. The temperature was kept constant within the limits of ±2° with the help of a contact thermometer. Pressure was developed with a pump (up to 650 atm) and a hydraulic compressor; in experiments at pressures up to 1400 atm the reactor was first charged with the experimental mixture, and then benzene was pumped in to the required pressure with the pump or compressor. In experiments at pressures exceeding 1400 atm, the mixture was placed in a sealed lead ampoule and the pressure was developed with the help of a solution of water in glycerol which was pumped into the reactor with the hydraulic compressor. The reactor was heated for a period of 50-60 minutes; cooling was effected more slowly: in two hours after termination of heating the reactor had been cooled to 50°. The duration of an experiment (τ) was taken to be the period during which the reactor was at the specified temperature. After cooling and opening the reactor, its contents (or the contents of the lead ampoule) were poured onto ice; after the ice had melted, the product was extracted with ether, washed with water until neutral (removal of HCl), and dried over calcined sodium sulfate. The ether was then driven off, likewise the benzene (in a water bath) to a residual pressure of 20-25 mm). The liquid residue was weighed and fractionated in vacuum (1-2 mm) until the residue only contained resins which decomposed on further heating.

Variation of Yield of Products of Reaction with Pressure

In Tables 1 and 2 are presented the results of experiments on the reaction of benzene with anhydrous $AlCl_3$. The following conclusions can be drawn:

1) The total yield of reaction products increases with rising pressure.

2) Increase of pressure leads to a fall in the relative content of fractions boiling at lower temperatures (up to 140° at 1-2 mm).

These conclusions are generally applicable both for experiments performed directly in the reactor and for those in lead ampoules, notwithstanding the slight differences in the results of each of these series of experiments. These differences may have arisen from partial reaction of the released hydrogen chloride with the lead ampoule, resulting in formation of H_2 and $PbCl_2$. The amounts of lead chloride formed in Experiments 16 and 21 of the lead ampoule series were respectively 2.9 and 2.5 g.

*Mechanic V.A.Kuznetsov collaborated.

TABLE 1

Reaction of Benzene with $AlCl_3$ in a Stainless Steel Reactor at 100°

Expt. No.	C_6H_6 (g)	$AlCl_3$ (g)	τ (hrs)	P (atm)	Yield of products (wt.% of benzene)	Wt.% of fractions *			Notes
						up to 140°	140–170°	above 170°	
13	78.6	105.5	5	1 8 **	10.0	28.8	20.2	22.2	Fractionation to 215°
14	77.9	106.0	5	1.8 **	12.0	23.4	18.3	28.7	Fractionation to 213°
7	85.7	110.0	2	650	25.0	19.3	22.0 ****		
8	80.0	110.0	5	650	28.0	15.9	13.0	44.0	Fractionation to 240°
10	79.7	109.8	5	1400	24.0	6.8	9.6	62.0	Fractionation to 230°

TABLE 2

Reaction of Benzene with $AlCl_3$ in Lead Ampoules

Expt. No.	C_6H_6 (g)	$AlCl_3$ (g)	τ (hrs)	t_r	P (atm)	Yield of products (wt. % of benzene)	Wt.% of fractions*			Notes
							up to 140°	140–170°	above 170°	
21	44.9	59.9	5	100	1.8 **	10.2	17.0	17.2	29.4	Fractionation to 190°
16	45.0	60.5	2	100	2400	31.2	7.6	18.0	41.1	Fractionation to 243°
15 ***	9.24	11.0	2	120	3300	42.2				

* Fractionation at 1-2 mm mercury.

** Pressure of saturated benzene vapor at 100°.

*** Experiment carried out in a pressure apparatus.

**** Up to 180°.

Investigation of Composition of Reaction Products

The fractions obtained in Experiments 7 and 8 (Table 1), which were conducted at 100° and 650 atm, were subjected to two fractionations in succession at 1.2 mm. Only one crystalline substance was separated in this manner. We combined the crystals of this substance with those obtained in other experiments, separated them from oil with petroleum ether, filtered, and recrystallized them from benzene until the m.p. was constant.

The substance obtained is in the form of white needles with m.p. 156°, soluble in benzene, alcohol, and ether, and insoluble in water. Found %: C 93.62, 93.49; H 6.52, 6.58; M 209 (by Rast's method).

The composition, molecular weight and melting point correspond to those of 1,4-diphenyl-1,3-cyclopentadiene (m.p. 157-158°).

We prepared the picrate of this substance; m.p. (with decomposition) 145-146°, agreeing with that of the picrate of 1,4-diphenyl-1,3-cyclopentadiene [5].

Found %: C 51.30, 51.37, H 2.84, 3.02. $C_{29}H_{22}O_{14}N_6$. Calculated %: C 51.48; H 2.98.

Qualitative tests [5] were carried out (red solution with blue fluorescence in conc. sulfuric acid, yellow color of solution in mixture of chloroform and glacial acetic acid) and confirmed the identity of the substance with 1,4-diphenyl-1,3-cyclopentadiene.

The narrow fractions boiling below 180-190° (1.2 mm) were oily liquids whose viscosity increased with increasing boiling point; at temperatures above 190° an extremely viscous, dark-red oil came over and solidified to a vitreous mass in the receiver. Each of the fractions was analyzed for C and H and molecular weight (Rast), and the boiling points at atmospheric pressure were determined.

The first two fractions – 70-75° (1.2 mm) and 107-110° (1.2 mm) – were obtained in small quantities. Analyses of these fractions gave the following results:

1st Fraction 70-75° (1.2 mm). Found %: C 91.17, 90.87; H 9.05, 9.29.
2nd Fraction 107-110° (1.2 mm). Found %: C 91.91, 91.76; H 8.07, 8.16.

In Table 3 are set forth the results of examination of the higher boiling fractions together with the constants [6] of the assumed components of the mixture.

Examination of Table 3 indicates that Fraction 3 resembles diphenylcyclopentane whose presence was to be expected on the basis of examination of the crystalline product of the reaction (see Table, next page). In this fraction, however, there is also evidence of the presence of diphenylcyclohexane (and methyldiphenylcyclopentane). The constants of Fractions 5 and 6 are close to those of, respectively, triphenylcyclopentane and triphenylcyclohexane; Fraction 4 is apparently intermediate. Concerning Fractions 1 and 2 (see next page), they are evidently a

TABLE 3

Comparison of Results of Examination of Fractions with the Constants of the Assumed Components of the Mixture

Substance (or fraction)	B.p. (°)	C (%)	H (%)	M
Third fraction	300-306 (760)* 130-132 (1.2)	91.87, 91.88	8.36, 8.36	242
1,3-Diphenylcyclopentane	140-141 (3)	91.84	8.16	222
1,3-Diphenylcyclohexane	196-198 (17)			
1,4-Diphenylcyclohexane	190 (29)	91.53	8.47	236
Methyldiphenylcyclopentane	No data			
Fourth fraction	323-326 (760) 145-147 (1.2)	92.35, 92.25	7.92, 8.01	260, 268
Fifth fraction	330-340 (760) 165-170 (1.2)	92.93	7.34	287
1,2,4-Triphenylcyclopentane	285 (50)	92.62	7.38	298
Sixth fraction	360-380 (760) 190-200 (1.2)	92.24, 92.49	7.57, 7.69	308, 332
Triphenylcyclohexane. . . .	No data	92.32	7.68	312

*The pressure in mercury is given in brackets

mixture of phenylcyclohexane (or methylphenylcyclopentane) with the components of Fraction 3, although the composition of Fraction 2 is remarkably close to that of Fraction 3.

The experimental data thus justify the assumption that phenylated cyclohexanes and cyclopentanes are present in the reaction products.

DISCUSSION OF RESULTS

The foregoing data for the benzene–aluminum chloride interaction at pressures up to 3300 atm testify to the very great diversity of the reactions involved. These reactions evidently proceed within the complex constituted by the starting materials but may also involve hydrogen chloride. Without entering into speculation about the mechanism of the action of hydrogen chloride, we may point out that at the present time there is no doubt about the formation of a reactive complex in other similar reactions. Our data correlating the product yield with pressure show that the formation of the reactive complex and the sum total number of reactions taking place are accompanied by a reduction in volume. This was also to be expected because these reactions result in the formation of higher molecular hydrocarbons, and the hydrogen evolved during condensation is partly consumed in the hydrogenation of these hydrocarbons.

It must be noted that the increase of total yield of products with rising pressure is extremely significant (the increase is threefold with rise of pressure from 1.8 atm to 2400 atm). It is natural that the biggest increase in yield should apply to the hydrocarbons of highest molecular weight whose formation proceeds with maximum contraction in volume; this finds expression in our observation of the fall in the relative content of the lower boiling fractions in the reaction products.

SUMMARY

1. The effect of pressure up to 3300 atm on the interaction of benzene with anhydrous aluminum chloride has been investigated. Increase of pressure brings about a marked increase in the total yield of products and also increases the relative content of higher molecular products.

2. The products of interaction of benzene with anhydrous aluminum chloride under pressure were examined. Crystalline 1,4-diphenyl-1,3-cyclopentadiene was isolated and identified. The isolated liquid fractions resemble phenylated cyclohexanes and cyclopentanes in respect of chemical composition, boiling point and molecular weight.

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CHEMICAL REACTIONS AT EXTREMELY HIGH PRESSURES

II. REACTION OF BENZENE WITH CARBON DIOXIDE

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In 1931 Kinney and Langlois reported [1] that they had succeeded in preparing a small quantity of benzoic acid (0.13% of the weight of starting benzene) by heating benzene with CO_2 for 10 hours at 300° and 35 atm in presence of a catalyst of the type of Zn-Cu-Cr oxides. Subsequently (in 1935), however, in a paper by Kinney and Bonner [2] these results were described as erroneous on the basis of the authors' thermodynamic calculation of the equilibrium in the reaction:

$$C_6H_6 + CO_2 \rightleftarrows C_6H_5COOH. \qquad (1)$$

They stated that at 25°, ΔF = 4300 cal/mole (log K = −3.1), while at 250° ΔF = 18170 cal/mole (log K = −7.6).

The reaction of formation of benzophenone is even less advantageous from the thermodynamic viewpoint. Thus, at 25° the ΔF of this reaction is about 7 kcal/mole, i.e. K is about 10^{-5}. We have performed an approximate calculation of the effect of pressure on the equilibrium constant of reaction (1).

Data for the compressibility of CO_2 at pressures up to 3000 atm in the temperature range of 0-150° are given by Michels and co-workers [3]. From these data Michels calculated in another paper [4] the free energy of carbon dioxide under pressure. Without going into the details of our own calculations, we may limit ourselves to saying that this calculation was based upon an extrapolation of Michels' data into the region of higher temperatures and pressures. One result of this procedure was that the isochores of carbon dioxide at 0-150° and at densities of 0.9-1.2 g/cm³ were nearly rectilinear; this fact permitted easy extrapolation of P-V-T data at high pressures into the higher temperature region with the help of the formula:

$$P_T = P_{T_0} + a(T-T_0) \quad (\rho = \text{const.}).$$

The computations lead to the conclusion that at 300° and 5000 atm the equilibrium constant of the reaction of formation of benzoic acid from benzene and CO_2 is roughly 10^{-4}. Consequently the theoretical yield of benzoic acid even under super-high pressures is negligibly small.

On the other hand, Friedel and Crafts [5] long ago observed the formation of small amounts of benzoic acid after passing dry carbon dioxide through a mixture of benzene and anhydrous aluminum chloride heated nearly to boiling. At the same time a little hydrogen chloride was evolved. The authors suggested the formation of the compound $C_6H_5COOAl_2Cl_5$, which by reaction with water splits up to form benzoic acid.

In the patent literature [6] is described the preparation of benzoic acid by heating benzene with carbon dioxide in presence of anhydrous $AlCl_3$ (50% of the weight of the benzene) at 100° and 60 atm for 12-15 hours while stirring. According to the patent data the benzoic acid yield reaches 15% of the weight of starting benzene.

Our investigation had two main fields of inquiry:

1) Interaction of benzene with carbon dioxide at super-high pressures in the absence of catalysts.

2) Effect of pressure on the reaction of benzene with carbon dioxide in presence of anhydrous aluminum chloride.

Investigation of the Reaction of Benzene with Carbon Dioxide at Super-High Pressures in Absence of Catalysts

Theoretical data were presented above to illustrate the extremely low equilibrium concentrations of benzoic acid when prepared from benzene and CO_2 even at very high pressures. We undertook a series of experiments in a super-high pressure apparatus with the aim of establishing whether this reaction proceeds in the absence of a catalyst.

a) Experiments in steel ampoules with a moving piston. At first experiments were performed in a pressure apparatus* with a 15 cm^3 reactor capacity (Figure 1) into which was introduced an ampoule containing benzene and CO_2 and equipped with a moving piston (Figure 2). The ampoule was first placed in a Dewar flask containing a mixture of solid carbon dioxide and ether and then charged with solid carbon dioxide (1-2 g) and solid benzene (2-3 g). The ampoule was then closed with the piston and hollow nut and placed in the reactor of the pressure apparatus, after which pressure was developed in the reactor by means of a solution of water in glycerol. Experiments were performed at pressures of 7-8 thousand atm and temperatures of 125-200° over a period of 5 hours. Under these conditions no reaction of benzene with CO_2 was observed.

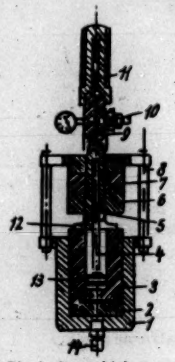

Fig. 1. Super-high pressure apparatus, 1) low-pressure cylinder; 2) packing of cylinder piston; 3) cylinder piston; 4) high-pressure piston; 5) packing of high-pressure cylinder; 6) reinforcing rings; 7) high-pressure cylinder; 8) column; 9) fitting to 12,000 atm pressure gage; 10) valve for feeding liquid into pressure apparatus; 11) reactor; 12) flange for connecting high-pressure cylinder to low-pressure cylinder; 13) packing of piston 4; 14) union for transmission of pressure to cylinder 1.

b) Experiments in a moving-piston reactor (without ampoule). The reactor was fitted with a moving piston and a valve for feeding gas; experiments were then performed in it at pressure up to 8-9 thousand atm and temperatures of 150-175° for 5 hours. The charge of benzene was here increased to 4.8-5.3 g. No products of interaction of benzene with CO_2 were detected.

c) Experiments in a large reactor. Experiments carried out in the pressure apparatus with a large reactor (approx. 50 cm^3) at 5-6 thousand atm and 125-150° for 5 hours likewise did not yield positive results. Finally, it was deemed necessary to try the effect of stirring of the mixture at super-high pressures.

Fig. 2. Ampoule with moving piston. 1) moving piston 2) stop nut.

d) Experiments in a rocking reactor. (Figure 3) were conducted at pressures up to 4500 atm and temperatures of 200 and 300°. At first the reactor was filled with dry carbon dioxide (dried in a high-pressure bomb over calcium chloride). Pressure was then created in the reactor by pumping in a mixture of dry, cryoscopically pure benzene and absolute ethanol or methanol; the pressure was then increased with the help of an intermediate vessel connected to a hydraulic compressor (Figure 4). Utilization of alcohols was necessitated by the solidification of pure benzene at pressures of about 900 atm at room temperature. It was established in preliminary experiments that benzene does not react with ethyl or methyl alcohol in the absence of a catalyst at pressures up to 6000 atm and temperatures of 200-300°.

The rocking reactor experiments likewise failed to yield positive results.

Consequently we were unable to establish the formation of benzoic acid or benzophenone from benzene and carbon dioxide at super-high pressures in absence of catalysts.

Investigation of Reaction of Benzene with Carbon Dioxide Under Pressure In Presence of Anhydrous Aluminum Chloride

We performed experiments in the rocking reactor (Fig. 3) constructed of stainless steel, capacity 130 cm^3, at pressures up to 2000 atm and at 100°. The reactor was charged with aluminum chloride and benzene, after which carbon dioxide (dried over calcium chloride in a high-pressure bomb for several days) was added. This

* The pressure apparatus was constructed in collaboration with L. F. Vereshchagin with assistance from Engineering Draughtsman A. A. Opekunov.

resulted in a pressure in the reactor of 80-100 atm ($P_{initial\ CO_2}$). Then with the help of a pump or intermediate vessel (Fig. 4) a definite amount of benzene was pumped into the reactor until the required initial pressure ($P_{initial}$) was attained, following which the electric heater of the reactor was switched on. The duration of the experiment (τ) was reckoned to be from the moment of attainment of the required temperature (100°) to the switching-off of the heat.

After the reactor had cooled, the product was poured on to ice, extracted with ether, washed with water, and treated with 10% KOH solution; the alkaline solution was then separated and acidified with dilute hydrochloric acid. The separated residue of benzoic acid was filtered off and dried. The benzoic acid obtained had m.p. 107-110°. After recrystallization and sublimation it melted at 119-120°.

The ether solution was again washed with water until neutral and dried over calcined sodium sulfate; the ether was then driven off, followed by the benzene (in a water bath to a residual pressure of 20-25 mm). The residue (liquid product) was weighed and fractionated in vacuum at 1-2 mm. The 115-140° fraction was predominantly benzophenone. A second distillation of this fraction gave the benzophenone in the form of crystals identified by the preparation of the phenylhydrazone with m.p. 131-133° (the literature gives 134°).

The higher boiling fractions were hydrocarbons — products of reaction of benzene with anhydrous $AlCl_3$ [7], including crystalline 1,4-diphenyl-1,3-cyclopentadiene.

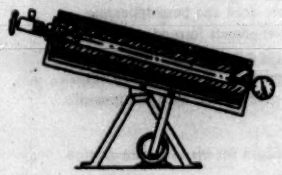

Fig. 3. Rocking reactor.

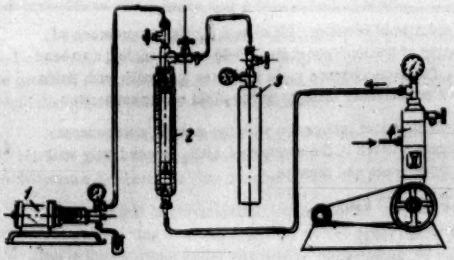

Fig. 4. Scheme for charging rocking reactor. 1) pump; 2) intermediate vessel; 3) rocking reactor; 4) hydraulic pump as designed by L. F. Vereshchagin

We may draw the following conclusions from the table:

1) Increase of pressure above 70-80 atm leads to an insignificant increase in the benzoic acid yield and to a more appreciable increase in the benzophenone yield.

2) An increase in the amount of anhydrous aluminum chloride causes a marked rise in the benzophenone yield.

DISCUSSION OF RESULTS

The above experimental data, together with the literature data, indicate that in the reaction of benzene with carbon dioxide in presence of anhydrous aluminum chloride, the latter enters into the reaction and thereby brings about the possibility of obtaining benzoic acid and benzophenone in yields many times greater than the equilibrium concentrations of these products as calculated from the change of free energy in the forward reactions: $C_6H_6 + CO_2 \rightleftarrows C_6H_5COOH$ and $2C_6H_6 + CO_2 \rightleftarrows (C_6H_5)_2CO + H_2O$.

The effect of pressure on the course of the reaction between benzene and CO_2 in presence of $AlCl_3$ is, evidently, especially marked at low pressures when the density of the carbon dioxide sharply increases. Thus, according to the patent data [6] the passage of CO_2 for 30 hours through boiling benzene (600 g) in presence of 135 g $AlCl_3$ leads to the formation of 1.2 g C_6H_5COOH in all, while at 50 atm under the same conditions 40 g (i.e. 6.7%) benzoic acid and 4 g (0.7%) benzophenone are obtained. Our experiments showed that further increase of pressure has a very much weaker effect upon the benzoic acid yield; however, the benzophenone yield rises more appreciably

Interaction of Benzene with Dry Carbon Dioxide in Presence of $AlCl_3$ at 100° and τ = 5 hours

Expt. No.	C_6H_6 (g)	$AlCl_3$ (g)	Pressure			Yield (wt. % of benzene)			
			Initial CO_2 pressure in atm	Initial in atm	Mean in atm	C_6H_5COOH	Liquid products	Benzophenone fraction	Benzophenone
26a	40	20	40	40	78	6.0	16.3	3.5	3.0
38	73	40	95	320	620	5.9	24.2	8.8	7.8
37	75	40	100	375	900	6.5	23.1	11.7	8.4
39	73	40	90	490	1300	7.5			
42	77	40	90	850	2000	7.2	23.9	9.3	8.2
34	90	20	63	200	570	4.3	6.7	2.2	1.9
36	90	20	94	360	1270	3.7	6.6	2.5	2.1
43	75	50	80	600	1550	5.2	32.3	14.9	13.2

with the pressure than does the benzoic acid yield. We do not yet possess sufficient data to establish whether benzophenone formation proceeds through benzoic acid as intermediate product or whether it is an independent parallel reaction. It is more probable, however, that the formation of both benzoic acid and benzophenone occurs at the instant of decomposition of the respective complexes or chemical compounds formed with aluminum chloride. It is natural to assume that the formation of this type of complex (or compound), involving not one but two phenyl radicals, will be accompanied by a large contraction in volume, and this would also result in the much greater increase in the yield of benzophenone with rising pressure in comparison with the benzoic acid yield.

In conclusion the authors express their sincere thanks to Dr. L. F. Vereshchagin for his valuable advice in the completion of this investigation.

Mechanic V. A. Kuznetsov took part in the investigation.

SUMMARY

1. An investigation has been made of the system benzene-carbon dioxide at super-high pressures (up to 9000 atm) and elevated temperatures. No products of chemical interaction of the starting components could be detected.

2. The effect of pressures up to 2000 atm on the reaction of benzene with carbon dioxide in presence of anhydrous aluminum chloride was examined. Application of pressures exceeding 70-80 atm was found to lead to an insignificant increase in the benzoic acid yield. The benzophenone yield increases markedly with rising pressure. Increasing $AlCl_3$ content is accompanied by a considerable increase in the yield of benzophenone.

It was confirmed that aluminum chloride enters into chemical interaction with the starting components, and this fact indicates the possibility of performing reactions which in the absence of $AlCl_3$ proceed only with negligible yields under the investigated conditions of temperature and pressure.

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PROPERTIES OF 2-METHYL-4-PHENYL-2-PENTEN-4-OL OXIDE

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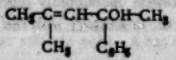
For the preparation of 2-methyl-4-phenyl-2,3-pentadiene we selected the Grignard reaction between mesityl oxide and phenyl magnesium bromide. This reaction has already been studied twice.

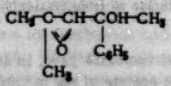
Klages [1] showed that mesityl oxide reacts normally with C_6H_5MgBr; however, in place of the unsaturated tertiary alcohol he obtained the product of its dehydration, 2-methyl-4-phenyl-2,3-pentadiene. Esafov [2] performed this reaction under very drastic conditions when the unstable reaction products undoubtedly suffered modification, and he obtained neither alcohol nor hydrocarbon; he also drew an incorrect conclusion about the course of the reaction.

Under our conditions the reaction proceeded normally and we obtained the unsaturated alcohol, 2-methyl-4-phenyl-2-penten-4-ol:



(I)

in yields of up to 70% of the calculated amount. We oxidized this alcohol with acetyl hydroperoxide with the aim of studying the properties of the alcohol-oxide:



(II)

since very few examples of such compounds are known and their properties have been inadequately studied.

α-Oxides are known to be characterized by addition reactions and by isomerization due to the cleavage of the oxide ring. The velocity of these processes, however, varies for α-oxides of different structures. For example, more energetic hydration takes place in the case of α-oxides whose oxide ring includes a tertiary carbon atom [3], while isomerizations to the corresponding aldehydes or ketones are more rapidly performed with α-oxides to whose oxide ring a phenyl radical is attached [4].

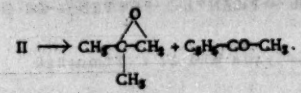
In his classic investigations of α-oxides, N. A. Prilezhaev [5] points out that the oxide ring of alcohol-oxides is stabilized by the hydroxyl group if the latter is in the α,β-position to the oxide ring. Hydration of the geraniol and linalool dioxides prepared by him only proceeded at the oxide ring remote from the hydroxyl group, and glyceryl oxides were then formed.

It must be pointed out that N. A. Prilezhaev also drew attention to a completely anomalous example -- the oxide of allyl alcohol [6] which is readily hydrated to a glycerol. He explains this by the general rule of the difference between the first member of a series and its homologs.

In the present communication we describe an α-oxide which contains sharply contrasting functional groups. The oxide ring contains a tertiary carbon atom, susceptible to hydration; in the α,β-position to the oxide ring is the hydroxyl group which inhibits hydration; finally, the molecule of the alcohol-oxide contains a phenyl radical susceptible to the isomeric transformations of α-oxides. Such a diversity of functional groups in the alcohol-oxide prepared by us was clearly reflected in the properties of the α-oxide.

2-Methyl-4-phenyl-2-penten-4-ol was oxidized with 69.8% acetyl hydroperoxide in absolute ether. From the oxidation products was separated a crystalline substance with m.p. 55-56° whose analysis confirmed the presence of the alcohol-oxide (II). This compound proved to be extraordinarily unstable even at the ordinary temperature. A portion of the crystals of the alcohol-oxide was placed in a box in a desiccator over sulfuric acid for drying. After 7 days the whole of the material had been transformed into an oily liquid with the odor of acetophenone, which substance was also identified through the semicarbazone. No other decomposition product could be identified.

Over P_2O_5 and $CaCl_2$ the alcohol-oxide likewise broke down to acetophenone and a volatile substance with a rather sharp odor. This substance was apparently isobutene oxide, for the breakdown of our alcohol-oxide may be represented, by analogy with the known cleavage of some pinacones [7], by the following scheme:

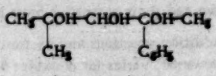


With the aim of identifying the second product of cleavage of the alcohol-oxide, we heated it in a Wurtz flask. Decomposition commenced at 200° with separation of a readily volatile substance with an unpleasant odor of rancid fats. The first distillates from the decomposition products gave a silver mirror, a semicarbazone with m.p. 124-125° and a crystalline product of condensation with dimedon melting at 151-152°. The analytical data for these crystals corresponded to the product of condensation of dimedon with isobutyraldehyde. The second product was acetophenone. This confirmed the foregoing scheme, for the isobutyraldehyde in the present case was undoubtedly the product of isomerization of 2-methylpropene oxide when heated.

The alcohol-oxide also fairly rapidly decomposed at room temperature when placed in dilute sulfuric acid. This was evident from the odor of the isobutyraldehyde formed. A second product, again, was acetophenone. Formation of isobutyraldehyde in sulfuric acid solution likewise undoubtedly proceeded via 2-methylpropene oxide and a series of intermediate reactions with sulfuric acid, in analogy with the behavior of ethylene oxide [8].

The alcohol-oxide also decomposed in semicarbazide solution, always forming acetophenone semicarbazone but no isobutylraldehyde semicarbazone. The absence of the latter is in accord with the findings of K. A. Krasusky [9] who reported that 2-methylpropene oxide does not isomerize to isobutyraldehyde in alkaline and neutral media.

Oxidation of 2-methyl-4-phenyl-2-penten-4-ol with acetyl hydroperoxide gave, in addition to the crystalline alcohol-oxide, a considerable amount of liquid product, probably the acetate of the trihydric alcohol,



We did not succeed, however, in isolating the pure substance since on vacuum distillation (4 mm) it broke down to acetophenone.

EXPERIMENTAL

Preparation of 2-methyl-4-phenyl-2-penten-4-ol (I). Into the 24 g magnesium in ether was slowly poured 152 g bromobenzene. At the conclusion of the reaction the mixture was heated for 30 minutes, and then, with ice-water cooling, 100 g mesityl oxide was poured in. The reaction mixture was again heated on the water bath for 30 minutes and left until the next day. By that time the flask contained a considerable amount of crystals and the ethereal solution had a yellow-orange color. The contents of the flask were cooled with ice-water and decomposed, first with a large amount of ice and then with dilute (1:3) sulfuric acid. The ether layer was separated and the aqueous layer subjected to two ether extractions. After drying over potassium carbonate, the ether was driven off and the substance (222 g) distilled at 20 mm to give the following fractions: I) 63-107° (24 g); II) 107-124° (17 g); III) 124-130° (133 g); IV) 130-140° (19 g); V) residue in flask (19 g).

In view of the fact that distillation at 130-140° (20 mm) was accompanied by appreciable decomposition of the substance with evolution of water, a second distillation of the third fraction was effected at 2 mm, at which pressure the substance came over at 91-92°.

n_D^{19} 1.5292; d_4^{19} 0.9777; MR_D 55.53; calculated 55.07.

0.1901 g substance: 0.5699 g CO_2; 0.1503 g H_2O. 0.1987 g substance: 24.39 ml CH_4 (0°, 760 mm). 0.1399, 0.2790 g substance; 19.53 g benzene: Δt 0.220°, 0.442°. Found %: C 81.76; H 8.84; OH 9.37; M 167.3, 166.1. $C_{12}H_{16}O$. Calculated %: C 81.82; H 9.09; OH 9.66; M 176.

Oxidation of 2-methyl-4-phenyl-2-penten-4-ol with acetyl hydroperoxide. 60 g alcohol in 100 ml absolute ether was oxidized with 38 g of 69.86% acetyl hydroperoxide. Oxidation proceeded

energetically with heat development, for which reason the hydroperoxide was added in small portions as the reaction progressed, and the reaction mixture was cooled with cold water. The temperature was held at 20-25°. At the end of one hour after completion of the addition, the reaction mixture contained 2.7 g unreacted hydroperoxide, and this amount was still unchanged on the following day. The whole mixture was therefore neutralized with 10% sodium carbonate, and then with dry sodium carbonate. The ether solution was dried over Na_2SO_4 and filtered; the ether was partly driven off and the residue retained for crystallization, a preliminary experiment having indicated the presence of a crystalline substance. After 4 days, 18.0 g white acicular crystals with the odor of camphor was obtained. The substance was very easily soluble in benzene, chloroform, carbon tetrachloride, methyl alcohol, ethyl alcohol, petroleum ether and other solvents. On recrystallization from ethyl alcohol it melted at 55-56°.

0.1879 g, 0.1963 g substance: 0.5177 g, 0.5388 g CO_2; 0.1438 g, 0.1488 g H_2O. 0.1727 g substance: 19.35 ml CH_4 (0°, 760 mm). 0.2095 g, 0.3781 g substance; 22.59 g benzene: Δt 0.236°, 0.468°. Found %: C 75.09, 74.86; H 8.56, 8.50; OH 8.54; M 181.2, 184.2. $C_{12}H_{16}O_2$. Calculated %: C 75.0; H 8.33; OH 8.85; M 192.

Distillation of the liquid products of oxidation (28.5 g) at 4 mm gave: I) 72-83° (10.4 g), n_D^{20} 1.5232; II) 83-105° (2.0 g), n_D^{20} 1.5239; III) 105-120° (5.3 g), n_D^{20} 1.5290; IV) resinous residue (10.8 g). The substance in the first three fractions was acetophenone. At the ordinary pressure it distilled at 198-200°; it gave a semicarbazone with m.p. 197-199° which did not depress the melting point of acetophenone semicarbazone.

Cleavage of the alcohol-oxide over sulfuric acid. 1.5 g of the alcohol-oxide was placed in a desiccator over sulfuric acid. After two days there was appreciable formation of a liquid product with the odor of acetophenone, and after 7 days no crystals of the oxide remained. The liquid product boiled at 3 mm pressure at 61-63° and at the ordinary pressure at 200-202°.

n_D^{20} 1.5220; d_4^{20} 1.0431; MR_D 35.5. C_8H_8O; calculated 35.08.

The substance gave a semicarbazone with m.p. 198-199° which did not depress the m.p. of authentic acetophenone semicarbazone. We were unable to isolate other products of the cleavage of the alcohol-oxide, although a readily volatile substance was undoubtedly present, as indicated by the frothing of the liquid at the start of distillation in vacuum.

Cleavage of the alcohol-oxide over $CaCl_2$ and P_2O_5. Two lots of 2.0 g of alcohol-oxide crystals were placed in separate desiccators over $CaCl_2$ and P_2O_5 respectively. After a week both lots of crystals had been converted into liquid, and after 10 days they had completely disappeared. The air in the desiccators (containing a substance with a fairly sharp odor) was sucked through solutions of semicarbazide and dimedon, but neither a semicarbazone nor a dimedon condensation product was obtained. The liquid which had formed, smelling of acetophenone, distilled at 199-201° and gave a semicarbazone melting at 199-200° which did not depress the melting point of authentic acetophenone semicarbazone.

Cleavage of the alcohol-oxide by heating. 2.0 g of crystals of alcohol-oxide was heated in a flask over a bare flame. The crystals melted and then cleavage of the alcohol-oxide took place at 200°; the unpleasant odor of rancid fat was clearly evident. The first fractions from distillation came over at 70-100° and were collected in semicarbazide solution, dimedon and ammoniacal silver oxide solution. With the last-named a magnificent silver mirror was quickly formed. The solution of semicarbazide containing the cleavage product was heated on the water bath for about an hour, giving on cooling a semicarbazone melting at 124-125°, which agreed with the literature data [10] for isobutyraldehyde. The dimedon solution containing the aldehyde was heated for 3 hours on the water bath. Snow-white acicular crystals came down within few hours after cooling, and these melted (after recrystallization from ethyl alcohol) at 151-152°. Since the literature does not mention the product of condensation of isobutyraldehyde with dimedon, we carried out its analysis:

0.1580 g substance: 0.4141 g CO_2; 0.1260 g H_2O. Found %: C 71.48; H 8.92. $C_{18}H_{28}O_4$. Calculated %: C 71.85; H 8.98.

A second product distilled over at 198-200° and when collected in semicarbazide solution it gave a semicarbazone melting at 199-200°. It did not depress the melting point of authentic acetophenone semicarbazone.

Cleavage of the alcohol-oxide in sulfuric acid solution. 10 ml of 0.1 N sulfuric acid was poured into 1.6 g of the alcohol-oxide. In 15-20 minutes the odor of isobutyraldehyde was noticed and the crystals had been replaced by liquid. On the following day there was no trace of crystals. At the bottom

of the test-tube was a layer of oily substance with the odor of acetophenone, and a strong smell of rancid fat came from the test-tube. With semicarbazide the substance of the bottom layer gave a semicarbazone with m.p. 197-199°; it did not depress the m.p. of acetophenone semicarbazone. The second cleavage product, with the odor of isobutyraldehyde, was distilled into an alcoholic solution of dimedon. Heating for two hours, followed by cooling resulted in separation of snow-white acicular crystals which melted at 150.5-151°. No melting point depression occurred after mixing these crystals with those obtained by condensing dimedon with the product of cleavage of the alcohol-oxide by heating.

SUMMARY

1. Synthesis was effected from phenyl magnesium bromide and mesityl oxide of the unsaturated alcohol 2-methyl-4-phenyl-2-penten-4-ol in 75% yield.

2. Oxidation of 2-methyl-4-phenyl-2-penten-4-ol with acetyl hydroperoxide gave its oxide.

3. It was established that the oxide of 2-methyl-4-phenyl-2-penten-4-ol is extremely unstable. In a desiccator over H_2SO_4, $CaCl_2$ and P_2O_5, also on heating and in sulfuric acid solution, it splits up into acetophenone and 2-methylpropene oxide.

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SYNTHESIS OF METHYL p-TOLYLETHINYL CARBINOL AND ITS DERIVATIVES

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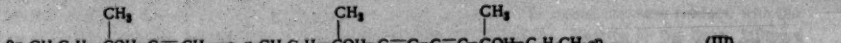
Propargyl alcohol, first prepared in 1872 [1], is the simplest representative of the homologous series of monohydric acetylenic alcohols. Other representatives of the series have been synthesized by very different methods. Tertiary acetylenic alcohols can be prepared in good yield by A. E. Favorsky's method [2] of condensation of various ketones with acetylene in presence of powdered potassium hydroxide. Relatively little attention has so far been given, however, to the reaction of acetylene with alkaryl ketones. We know that acetophenone does not react with acetylene in presence of powdered potassium hydroxide [3]. It was possible, however, to obtain 2% of methylphenylethinyl carbinol from acetophenone and acetylene in presence of sodium amide [4]. This yield could be increased to 7% by reacting acetophenone with sodium acetylide in liquid ammonia [5].

We decided to investigate the condensation of methyl-p-tolyl ketone with acetylene in presence of potassium hydroxide powder and to examine the influence of the p-tolyl radical on the velocity of this reaction. Preliminary experiments showed that methyl-p-tolyl ketone is more reactive than acetophenone when the reaction with acetylene is performed under the usual conditions. The main reaction product was di-p-tolyl-2,5-hexyne-3-diol-2,5 (II), in the form of three isomers with different melting points, together with a small amount of methyl p-tolyl-ethinyl carbinol (I) in admixture with the original ketone [6]. In this investigation we succeeded in raising the yield of methyl p-tolylethinyl carbinol to 50% by adopting the procedure of I. A. Favorskaya and L. V. Fedorova [7] of greatly increasing the dilution of the ketone with the solvent and decreasing the rate of its addition to the reaction mass. In this manner more favorable conditions were created for the formation of the acetylenic alcohol. But notwithstanding the great dilution and the rapid flow of acetylene, the product of the reaction always consisted of a mixture of methyl-p-tolyl-ethinyl carbinol (I), methyl p-tolyl ketone and dimethyl di-p-tolylbutyne diol (II):

$$n\text{-}CH_3C_6H_4COCH_3 + HC\equiv CH \longrightarrow \underset{-C_6H_4CH_3\text{-}n.}{n\text{-}CH_3C_6H_4\text{-}\overset{CH_3}{\underset{|}{C}}OH\text{-}C\equiv CH} \ (I) + \underset{(II)}{n\text{-}CH_3C_6H_4\text{-}\overset{CH_3}{\underset{|}{C}}OH\text{-}C\equiv C\text{-}\overset{CH_3}{\underset{|}{C}}OH\text{-}}$$

The mixture of products was subjected to distillation under reduced pressure when a liquid came over consisting of starting ketone and the acetylenic alcohol. The higher boiling fraction isolated by fractional distillation was treated with a solution of semicarbazide acetate (for removal of traces of the initial ketone) and then left in the cold for a long period when very large regular crystals came down. These melted, after purification, at 34-35°. The aqueous alcoholic solution of the crystals was decolorized with aqueous permanganate and gave a white precipitate with ammoniacal silver oxide solution. Results of carbon and hydrogen determinations, of molecular weight and molar refraction determinations (the latter in supercooled solution), and of the determination of the percent content of active hydrogen (Terentiev-Shcherbakova method) showed that we had actually obtained the acetylenic alcohol, methyl p-tolylethinyl carbinol. A weighed sample of the substance was hydrogenated in presence of platinum, when addition occurred of 102 % of hydrogen (on the theoretically calculated amount). Hydrogenation yielded a saturated alcohol, methylethyl p-tolyl carbinol, boiling at 99-100° (5 mm). Its principal constants were determined. For comparison the synthesis was then effected of authentic methylethyl p-tolyl carbinol from p-bromotoluene and methylethyl ketone. From methyl p-tolylethinyl carbinol (I) was obtained, by the method of Zalkind and Aizikovich [8] the corresponding diacetylenic glycol, di-p-tolyl-2,7-octadiyne-3,5-diol-2,7 (III). Formation of the glycol was only observed, however, after passage of an oxygen stream and after a few hours had elapsed following the addition of the methyl p-tolylethinyl carbinol. On driving off the ether, a crystalline mass remained which could be separated into two isomers: the first in the form of lustrous platelets which turned dull on standing and melted at 129-130°; the second in the form of needlets melting at 136-137°. The aqueous alcoholic solutions of both isomers were decolorized with aqueous permanganate. Each of the isomers was analyzed for content of carbon, hydrogen and active carbon. The results conformed to di-p-tolyl-2,7-octadiyne-3,5-diol-2,7 (III), which was obtained in about 82% yield:



Catalytic hydrogenation of the first isomer in presence of platinum resulted in the addition of 100.6% hydrogen with formation of a saturated glycol in the form of snow-white flakes with a pearly irridescence, melting at 77-78°. The analysis corresponded to di-p-tolyl-2,7-octanediol,2-7. Catalytic hydrogenation of the second isomer of di-p-tolyl-2,7-octadiyne-3,5-diol-2,7 in presence of platinum resulted in addition of 100.3% hydrogen with formation of a white, finely crystalline powder with m.p. 114.5-115.5°. Analysis of this saturated glycol showed it to correspond to another isomer of di-p-tolyl-2,7-octanediol-2,7.

It is known from the literature that the melting points of tertiary acetylenic alcohols and the corresponding starting ketones are nearly always close to one another. This is clearly illustrated by the table following. On the basis of these data it was possible to predict that the acetylenic alcohol obtained from methyl p-tolyl ketone (m.p. 28°) would have a low m.p. close to room temperature, and to infer that the m.p. of 120-121° given by Iremadze[12] for methyl p-tolylethinyl carbinol was extremely dubious. From our own results it is seen that Iremadze did not obtain methyl p-tolylethinyl carbinol when he reacted methyl p-tolyl ketone with acetylene, but a mixture of the isomers of di-p-tolyl-2,5-hexyne-3-diol-2,5 with which all the subsequent investigation was performed.

Starting ketones	M.p.	Literature	Acetylenic alcohols	M.p.	Literature
Acetophenone	20.5°	[9]	Methylphenylethinyl carbinol	49°	[10]
Benzophenone	49	[9]	Diphenylethinyl carbinol	44.5	[10]
Methyl p-tolyl ketone	28	[9]	Methyl p-tolylethinyl carbinol	34-35	[4,11]
Di-p-tolyl ketone	90-95	[7]	Di-p-tolylethinyl carbinol	86-87	[7]

EXPERIMENTAL

Preparation of methyl p-tolyldiethinyl carbinol. Into a three-necked flask fitted with a powerful propeller-type stirrer were introduced 250 g potassium hydroxide powder and 300 ml absolute ether. While a continuous stream of acetylene was passed in under external cooling with ice-water, addition was made to the reaction mass of 40 g methyl p-tolyl ketone in 600 ml absolute ether. The methyl p-tolyl ketone was prepared from methyl p-tolyl carbinol through p-toluidine and p-bromotoluene. The boiling point of the ketone (9 mm) was 94-95°. The ketone was added over a period of 10 hours. The reaction mass was left overnight and then decomposed with iced water. The separated ether layer was saturated with carbon dioxide and dried with sodium sulfate; the ether was then evaporated.

The residue was distilled in vacuum. Fraction I (12.0 g) boiled at 92° (7 mm), and at 96° (3 mm); fraction II (34.7 g) at 97° (3 mm); the residue in the flask (4.2 g) crystallized.

The aqueous alcoholic solution of the second fraction gave a precipitate with ammoniacal silver oxide solution and with aqueous permanganate solution. The liquid gave a precipitate with an acetic acid solution of semicarbazide. In order to remove traces of the original methyl p-tolyl ketone, the whole of the liquid product was treated with an acetic acid solution of semicarbazide, and the semicarbazone precipitate was filtered and recrystallized from alcohol. Its m.p. of 202-203° corresponded to that of methyl p-tolyl ketone semicarbazone. The filtrate was extracted with ether, and the ether extract washed with soda solution and dried with sodium sulfate. Removal of the ether left 22.7 g methyl p-tolylethinyl carbinol boiling at 103.5° (5 mm) and crystallizing on standing in the cold. The crystals melted at 34-35° (from petroleum ether with b.p. 40-60°). The crystals were 1-2 cm in length. The yield of acetylenic alcohol (allowing for the unreacted ketone) was 69.0% of theory.

$d_4^{20.0}$ 1.0066; d_4^{20} 1.0088; $n_\alpha^{19.8}$ 1.52832; $n_\beta^{19.8}$ 1.54271; n_D^{20} 1.5310; MR_α 49.03; MR_β 50.14; MR_D 49.13. $C_{11}H_{11}OF_3F$. Calculated MR_α 48.55; MR_β 49.71; MR_D 48.92.

0.1152 g substance: 0.3488 g CO_2; 0.0794 g H_2O. 0.1110 g substance: 0.3360 g CO_2; 0.0770 g H_2O. 0.0945 g substance; 18.00 g benzene: Δt 0.174°. 0.2288 g substance: 18.00 g benzene: Δt 0.422°. 0.1346 g substance: 20.7 ml CH_4 (20°, 763.1 mm). 0.1273 g substance: 18.4 ml CH_4 (20°, 763.1 mm). Found %: C 82.57, 82.55; H 7.71, 7.76; M 156.3, 156.0; active H-atoms 1.006, 1.008. $C_{11}H_{11}OH$. Calculated %: C 82.46;

H 7.51; M 160.2; active H-atoms 1.000.

Catalytic hydrogenation of methyl p-tolylethinyl carbinol. 5.00 g substance: 0.5 g Pt, 60 ml alcohol. Hydrogenation was performed for 1 hour 20 minutes.

Addition took place of 1425 ml H_2 (0°, 760 mm) equivalent to 101.5%. $C_{11}H_{12}O$. Calculated 1398.2 ml H_2.

After distilling off the alcohol there remained 4.1 g liquid boiling at 99-100° (5 mm) which did not form a precipitate with ammoniacal silver oxide solution and did not decolorize permanganate.

n_D^{20} 1.5158; d_4^{20} 0.9691; MR_D 51.16. $C_{11}H_{16}OF_2$. MR_D 50.92.

0.0941 g substance: 0.2783 g CO_2; 0.0814 g H_2O. 0.1069 g substance: 0.3157 g CO_2; 0.0932 g H_2O.
0.1800 g substance: 27.8 ml CH_4 (23.5°, 765 mm). 0.1318 g substance: 20.6 ml CH_4 (23.5°, 765 mm).
Found %: C 80.65, 80.54; H 9.68, 9.76; active H-atoms 1.019, 1.032. $C_{11}H_{16}OH$. Calculated %: C 80.45; H 9.82; active H-atoms 1.000.

Preparation of methylethyl p-tolyl carbinol. Methylethyl p-tolyl carbinol was prepared for comparison purposes from methylethyl ketone and p-bromotoluene. To 7.6 g Mg was added 53.5 g p-bromotoluene in 150 ml ether, and then 22.3 g methylethyl ketone in 50 ml ether. Removal of the ether left a residue of liquid boiling at 93-93.5° (3 mm).

n_D^{20} 1.5174; d_4^{20} 0.9726; MR_D 51.11. $C_{11}H_{16}OF_2$. Calculated MR_D 50.92.

0.1629 g substance: 0.4792 g CO_2; 0.1416 g H_2O. 0.1092 g substance: 0.3219 g CO_2; 0.0960 g H_2O.
0.1639 g substance: 25.7 ml CH_4 (17°, 760.6 mm). 0.1240 g substance: 20.0 ml CH_4 (17.5°, 760.6 mm).
Found %: C 80.23, 80.15; H 9.72, 9.84; H-atoms 1.075, 1.102. $C_{11}H_{16}OH$.
Calculated %: C 80.45; H 9.82; active H-atoms 1.000.

Analysis of di-p-tolyl-2,5-hexyne-3-diol-2,5. The solid residue after distillation of the methyl p-tolyl ketone and the methyl p-tolylethinyl carbinol amounted to 4.2 g and was recrystallized from benzene; it then melted at 121-123° and did not depress the melting point of a previously prepared and characterized mixture of the isomers of di-p-tolyl-2,5-hexyne-3-diol-2,5 [6].

0.1077 g substance: 18.3 ml CH_4 (18°, 749.6 mm). 0.1045 g substance: 18.1 ml CH_4 (18°, 749.6 mm).
Found: active H-atoms 2.024, 2.067. $C_{22}H_{26}(OH)_2$. Calculated: active H-atoms 2.000.

Preparation of di-p-tolyl-2,7-octadiyne-4,5-diol-2,7. 40 g Cu_2Cl_2 was mixed with 100 g NH_4Cl and to the mixture was added 400 ml water, 1.5 ml HCl and 10 g methyl p-tolylethinyl carbinol in 100 ml alcohol. The mixture was stirred in the course of 10 hours with continuous passage of a stream of oxygen (with a stream of air the diacetylenic glycol was formed only after several days). At the end of the day a white, clotted solid had formed at the surface of the mixture and was extracted with ether. The extract was dried over calcined potassium carbonate. The residue (after driving off the ether) was a syrupy liquid which crystallized on standing. After drying in the vacuum desiccator, the crystals melted at 106-111°. The amount was 8.1 g (81.5% of the theoretical yield). Repeated recrystallizations from benzene and from a mixture of benzene and petroleum ether (b.p. 40-75°) yielded two fractions of crystals: I) m.p. 129-130°, in the form of small scales; II) m.p. 136-137°, in the form of needlets.

Neither fraction gave a precipitate with ammoniacal silver oxide solution or decolorized an aqueous alcoholic solution of permanganate.

Analysis of the diacetylenic glycol with m.p. 129-130° (from benzene):
0.1075 g substance: 0.3282 g CO_2; 0.0679 g H_2O. 0.1105 g substance: 0.3372 g CO_2; 0.0702 g H_2O.
0.2857 g substance: 15.00 g dioxane: Δt 0.275°. 0.4104 g substance: 15.00 g dioxane: Δt 0.410°.
0.0819 g substance: 12.4 ml CH_4 (20°, 763.1 mm). 0.0796 g substance: 12.2 ml CH_4 (20°, 763.1 mm).
Found %: C 83.26, 83.22; H 7.07, 7.11; M 325.5, 313.6; active H-atoms 1.995, 2.019. $C_{22}H_{26}(OH)_2$.
Calculated %: C 83.05; H 6.96; M 318.4; active H-atoms 2.000.

Catalytic hydrogenation of ditolyloctadiynediol with m.p. 129-130°. 3.00 g substance: 1.4 g Pt, 70 ml alcohol. Duration of hydrogenation 2 hours 35 minutes. Addition occurred of 850.9 ml H_2 (0°, 760 mm), 100.8%. $C_{22}H_{22}O_2$. Calculated 846 ml H_2.

Removal of the alcohol left 2.9 g of a transparent viscous mass which crystallized in the course of three days. After two recrystallizations from petroleum ether (boiling range 40-75°) with a few drops of benzene, separation took place of crystals in the form of nacreous starlets with m.p. 77-78°. The obtained glycol did not decolorize an alcoholic solution of permanganate. A mixed sample with the original glycol melted at 107-122°.

0.1278 g substance: 0.3809 g CO_2; 0.1068 g H_2O. 0.1256 g substance: 0.3740 g CO_2; 0.1059 g H_2O. 0.1017 g substance: 14.8 ml CH_4 (21°, 762.1 mm). 0.1109 g substance: 15.6 ml CH_4 (21°, 760.1 mm). Found %: C 81.28, 81.21; H 9.35, 9.43; active H-atoms 1.862, 1.856, $C_{22}H_{26}(OH)_2$. Calculated %: C 80.94; H 9.26; active H-atoms 2.000.

Analysis of the diacetylenic glycol with m.p. 136-137° (from benzene-petroleum ether mixture).

0.1010 g substance: 0.3066 g CO_2; 0.0630 g H_2O. 0.1079 g substance: 0.3280 g CO_2; 0.0681 g H_2O. 0.0735 g substance: 11.0 ml CH_4 (20°, 763.1 mm). Found %: C 82.79, 82.90; H 6.98, 7.06. Found: number of active H atoms 2.000.

Catalytic hydrogenation of ditolyloctadiynediol with m.p. 136-137°. 0.70 g substance: 0.3 g Pt; 35 ml alcohol. Hydrogenation period 1 hr.5 min. Addition of 202.6 ml H_2 (0°, 760 mm), 100.3%, $C_{22}H_{22}O_2$. Calculated 197.0 ml H_2.

Removal of the alcohol left 0.7 g crude crystals. Recrystallization from a mixture of benzene and petroleum ether gave a white, powdery crystalline mass with m.p. 114.5-115.5°. A mixture with the original diacetylenic glycol melted at 100-105°; a mixture with the saturated glycol obtained from the first fraction melted at 70-100°.

0.1031 g substance: 0.3065 g CO_2; 0.0855 g H_2O. 0.0984 g substance: 15.6 ml CH_4 (23.5°, 765.3 mm). Found %: C 81.08; H 9.28; number of active H atoms 2.081. $C_{22}H_{26}(OH)_2$. Calculated %: C 80.94; H 9.26; number of active H atoms 2.000.

SUMMARY

1. Methyl p-tolyl ketone reacts with acetylene under Favorsky's reaction condition to give the tertiary acetylenic alcohol, methyl p-tolylethinyl carbinol, and the acetylenic glycol, symm. dimethyl di-p-tolylbutynediol.

The yields of alcohol and glycol vary with the reaction conditions, in particular the dilution and rate of addition of the methyl p-tolyl ketone.

2. Catalytic hydrogenation of methyl p-tolylethinyl carbinol in presence of platinum gave the saturated alcohol, methylethyl p-tolyl carbinol, which was characterized.

3. Methyl p-tolylethinyl carbinol can be converted by the method of Yu. S. Zalkind and M. A. Aizikovich into the diacetylenic glycol, di-p-tolyl-2,7- octadiyne-3,5-diol-2,5. Two forms of this glycol were isolated.

4. Catalytic hydrogenation of di-p-tolyl-2,7-octadiyne-3,5-diol-2,7 in presence of platinum gave two forms of the saturated glycol, di-p-tolyl-2,7-octadiol-2,7, which were characterized.

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ADDITION OF HYDROGEN TO ACETYLENE DERIVATIVES

INVESTIGATION OF THE VELOCITY OF HYDROGENATION OF 1,4-BUTYNEDIOL AND ITS ACETATE

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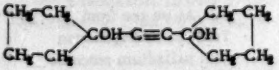
The catalytic hydrogenation of γ-acetylenic glycols, both ditertiary and disecondary, has been studied with reference to many substances by Yu. S. Zalkind and his pupils [1]. They showed that the velocity of hydrogenation of γ-acetylenic glycols in presence of colloidal palladium sharply slows down after addition of two atoms of hydrogen. This effect becomes increasingly marked with increasing radical length and molecular volume. In presence of platinum the velocity of hydrogenation falls off steadily without any discontinuity in the curve. Yu. S. Zalkind explained [2] the abrupt slowing-down of the reaction in the first case by closure of the ring by the hydrogen bond. After formation of the double bond, a ring is formed at the expense of the hydrogen of the hydroxyl groups which hinders access of the hydrogen atoms to the double bond.

The objective of the present investigation was the study of the velocity of hydrogenation of a substance in which no effect would be exercised by radicals, i.e. one in which steric hindrance would be excluded during the reaction. For this purpose we chose 1,4-butynediol and its acetate. This glycol has already [3] been hydrogenated both with platinum and palladium, but the authors were not interested in the velocity of hydrogen addition. According to the literature data, the hydrogenation of 1,4-butynediol proceeds more energetically when using palladium as catalyst (and ether as solvent) than when using platinum, and in the further course of hydrogenation the hydroxyl groups of the glycol are substituted by hydrogen with formation of a hydrocarbon. We have confirmed this process.

The experiments here performed have shown that the behavior of 1,4-butynediol is quite different from that of disecondary and ditertiary γ-acetylenic glycols. Firstly, it is hydrogenated very slowly (Table 1); secondly, in presence of colloidal palladium, after addition of two hydrogen atoms there is no discontinuity in the rate of addition.

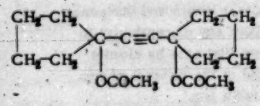
TABLE 1

Formula of the γ-glycols	Amount of palladium catalyst (in mg)	Amount of solvent (in ml)	Reaction temp.	Amount of glycol (in mole)	Period of addition of hydrogen (in minutes)
$CH_2OH-C\equiv C-CH_2OH$	10	50	20°	0.01	45
$CH_3-CHOH-C\equiv C-CHOH-CH_3$	5	50	24	0.01	6
$C_2H_5-CHOH-C\equiv C-CHOH-C_2H_5$	5	50	16	0.01	5
$(CH_3)_2COH-C\equiv C-COH(CH_3)_2$	5	50	18	0.01	10
$(C_2H_5)_2COH-C\equiv C-COH(C_2H_5)_2$	5	50	19	0.01	145 (78.4%)
	5	50	20	0.001	7

Regarding 1,4-butynediol acetate, the velocity of hydrogenation is here greater than for butynediol (Table 2); here also a discontinuity does not arise after addition of one molecule of hydrogen.

The results demonstrate that in the diprimary glycols, ring-closure by the hydrogen bond is excluded and the triple bond is more stable (due to the influence of the charged protons).

TABLE 2

Acetates of γ-acetylenic glycols	Amount of palladium catalyst (in mg)	Amount of solvent (in ml)	Reaction temp.	Amount of ester (in mole)	Period of addition of hydrogen (in min.)
$CH_3COOCH_2-C\equiv C-CH_2OOCCH_3$	5	50	26°	0.01	18
$CH_3-CH(OCOCH_3)-C\equiv C-CH(OCOCH_3)-CH_3$	10	50	14	0.01	5.5
$CH_3-C_6H_4-CH(OCOCH_3)-C\equiv C-CH(OCOCH_3)-C_6H_4-CH_3$	5	50	16	0.01	4 min.46 sec.
	5	50	18	0.01	9

Comparison of the rate of addition of hydrogen to 1,4-butynediol acetate with the rate of addition to other acetates of γ-acetylenic glycols shows that 1,4-butynediol acetate adds on hydrogen much more slowly (Table 2).

EXPERIMENTAL

Synthesis of butynediol acetate. A mixture of 10 g butynediol (m.p. 58°), 30 ml acetic anhydride and 1 g calcined sodium acetate was heated with constant stirring on the water bath at 98° for 13 hours. On pouring the reaction mass into water, an oily, brown-colored liquid was obtained which was washed with sodium bicarbonate solution and with water and then extracted with ether. After the ether had been evaporated, the substance distilled at 130-130.5° (14 mm) and consisted of a glycerol-like, colorless liquid. This crystallized on standing and formed transparent platelets with m.p. 31-32°. Yield 12 g or 42.4% of theory.

d_4^{20} 1.1265; n_D^{20} 1.4547; MR_D 40.92; calculated 40.45.

12.02 mg substance: 24.79 mg CO_2; 6.74 mg H_2O. 14.41 mg substance: 28.85 mg CO_2; 7.71 mg H_2O. 0.0904 g substance; 17.19 g benzene: Δt 0.155°. 0.019 g substance; 0.2344 g camphor: Δt 19.5°. Found %: C 56.29, 56.48; H 6.27, 6.18; M 164, 173.2. $C_8H_{10}O_4$. Calculated %: C 56.47; H 5.88; M 170.

Catalytic hydrogenation of 1,4-butynediol. Butynediol (m.p. 58°) which had been recrystallized from ether was hydrogenated in presence of colloidal palladium on wheat starch. The activity of the palladium was tested on tetramethylbutynediol which in presence of 5 mg of the palladium added on 2 atoms of hydrogen in the course of 12 minutes. Hydrogenation was also carried out with platinum black; ethyl alcohol was used as solvent. In Table 3 are set out the results of three experiments on glycol hydrogenation with 5, 10 and 20 mg palladium. The experiments were performed at 22°, using 50 ml of solvent (ethyl alcohol); in all of the experiments H_2 = 256 ml (quantity of hydrogen in milliliters required for conversion of an acetylenic glycol into an olefinic glycol); t = duration of experiment (in minutes).

TABLE 3

Expt. No.	Pd(in mg) \ t	3	6	9	12	15	18	21	24	27	30	33	36	51	102
1	5	20	32	43	52	61	70	79	88	97	106	115	134	–	271
2	10	41	61	79	96	116	130	147	161	175	188	201	–	–	279
3	20	40	68	94	118	142	166	189	211	233	255	275	–	–	–

As we see from Table 3, hydrogenation with palladium proceeds slowly and uniformly without any discontinuity. On interrupting the hydrogenation reaction in presence of palladium after combination of

two hydrogen atoms, an olefinic glycol is obtained in the form of a liquid boiling at 144-146° (21 mm); n_D^{20} 1.4700; d_{20}^{20} 1.0876; MR_D 23.26; calculated 23.25. The constants agree with the literature data.

Hydrogenation with platinum black (Table 4) also proceeds without a discontinuity; after addition of two hydrogen atoms (necessary to convert the triple bond into a double one) hydrogenation proceeded further at the expense of substitution of the hydroxyl groups.

TABLE 4 •

t . . .	3	6	9	12	15	18	21
v . . .	127	117	101	64	81	47	50
V. . .	127	244	345	409	537		
$2H_2$ (%)	25.1	48.2	68.2	80.8	96.8		

NOTE. t is the duration (in min. from start of experiment); v is the hydrogen vol. (in ml) absorbed during the preceding period; V is the volume absorbed from the start of the experiment.

Catalytic hydrogenation of 1,4-butynediol acetate in presence of colloidal palladium. Hydrogenation of the acetate (b.p. 130-131.5° at 14 mm) was effected under the same conditions as for 1,4-butynediol; the catalyst was from the same preparation. Table 5 gives the data for experiments with 5 and 10 mg of palladium. Temperature 26°; 50 ml ethyl alcohol for each experiment; H_2 = 262 ml (amount of hydrogen needed for conversion of the triple bond into the double one).

TABLE 5

Expt. No.	Pd (in mg) \ t	3	6	9	12	15	18	21	24	27	30	33	36
1	5	58	100	142	184	226	268	309	350	391	419	441	542
2	10	60	134	202	202	327	–	–	–	542	–	–	–

It is clear from Table 5 that hydrogenation proceeds uniformly without a discontinuity, and after addition of two molecules of hydrogen the reaction proceeds further, in all probability at the expense of reduction of the ester.

1,4-Butynediol acetate was also hydrogenated in presence of platinum black.

TABLE 6• •

t	3	6	9	12	15
v	110	180	159	139	64
V. . . .	110	290	449	588	652
$2H_2$ (%)	21	55.3	85.6		

Table 6 indicates that under the same conditions butynediol acetate is hydrogenated uniformly without any discontinuity and more rapidly than butynediol.

After addition of two atoms of hydrogen (in presence of palladium) the reaction was broken off. On working up the hydrogenation product, a colorless liquid (b.p. 128-129° at 25 mm) was obtained.

n_D^{20} 1.4430; d_{20}^{20} 1.0848; MR_D 42.04; calculated 41.98.

3.862 mg substance: 7.985 mg CO_2; 2.493 mg H_2O. 4.100 mg substance: 8.370 mg CO_2; 2.015 mg H_2O. 0.2268 g substance; 18.80 g benzene: Δt 0.345°. Found %: C 55.79, 55.71; H 7.22, 7.14; M 178. $C_8H_{12}O_4$. Calculated %: C 55.81; H 6.97; M 172.

After addition of two molecules of hydrogen the hydrogenation was broken off. The product was worked up to give a colorless liquid with b.p. 106-107° (10 mm).

n_D^{20} 1.4229; d_{20}^{20} 1.0559; MR_D 42.55; calculated 42.45.

4.411 mg substance: 8.855 mg CO_2. 3.172 mg H_2O. 4.353 mg substance: 8.760 mg CO_2; 3.100 mg H_2O. 0.2236 g substance; 18.00 g benzene: Δt 0.360°. Found %: C 55.78, 54.92; H 8.04, 7.97; M 174. $C_8H_{14}O_4$. Calculated %: C 55.17; H 8.04; M 177.2.

SUMMARY

1. Using 1,4-butynediol as an example, it was shown that a diprimary γ-acetylenic glycol in presence of colloidal palladium is hydrogenated more slowly than other γ-acetylenic glycols. No sharp slowing-down was observed after addition of two hydrogen atoms.

2. 1,4-Butynediol acetate has been synthesized for the first time. Its hydrogenation velocity in presence of palladium and platinum was investigated. 1,4-Butynediol acetate is found to hydrogenate more rapidly than

• 0.862 g substance; 0.736 g Pt; 50 ml ethyl alcohol; P 730 mm; T 21°; $2H_2$ = 506 ml.

•• 1.7 g substance; 0.736 g Pt; 50 ml ethyl alcohol; P 730 mm; T 21°; $2H_2$ = 524 ml.

1,4-butynediol. Hydrogenation proceeds at a uniform rate.

3. The products of hydrogenation of 1,4-butynediol acetate are described.

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144. HETEROCYCLIC COMPOUNDS. XX. STEREOISOMERISM IN THE HYDROGENATED THIOCHROMANONE SERIES. II.

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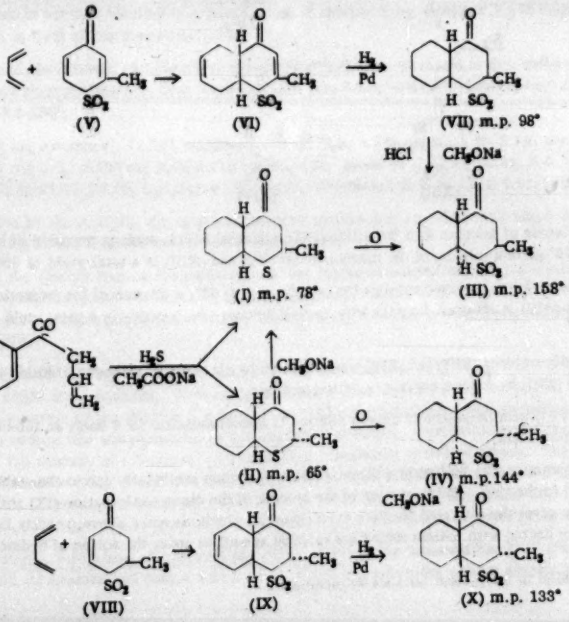
In a previous communication [1] we described a series of stereoisomers of hydrogenated derivatives of 2-methylthiochromanone, including three stereoisomeric bicyclic sulfones (III), (IV) and (VII).

In this investigation we synthesized a fourth and last stereoisomeric bicyclic sulfone (X). Consequently, all the possible stereoisomers of the dioxide of 2-methylhexahydro-1-thiochroman-4-one are now known and their structures have been established.

The previously obtained stereoisomeric bicyclic sulfones (III) and (IV) were synthesized by the action of hydrogen sulfide on allyl Δ^1-cyclohexenyl ketone in a weakly alkaline medium followed by oxidation of the stereoisomeric 2-methyl-hexahydro-1-thiochroman-4-ones (I) and (II) with potassium permanganate [2]. The third stereoisomeric bicyclic sulfone (VII) was obtained by condensation of the unsaturated monocyclic sulfone (V) with butadiene and subsequent reduction of the product of the diene synthesis (VI) in presence of Pd catalyst in a neutral medium.

The last stereoisomeric bicyclic sulfone (X) was obtained by condensation of butadiene with the unsaturated monocyclic sulfone (VII) followed by hydrogenation of the product of the diene synthesis (IX) in presence of Pd catalyst.



NOTE. The positions of the methyl groups are shown arbitrarily.

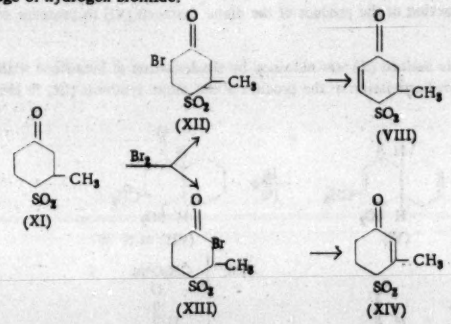
As was shown in the previous communication [1], the bicyclic sulfone (VII) isomerizes with extraordinary ease to the sulfone (III) under the influence of sodium methylate or hydrochloric acid. The bicyclic sulfone (X) also isomerizes to sulfone (IV) on boiling in dilute sodium methylate solution or on treating with hydrochloric acid.

The bicyclic sulfones (VII) and (X) possess a cis-configuration since they are obtained by the method of diene condensation, while the bicyclic sulfones (II) and (IV) belong, consequently, to the trans-series, as was confirmed by their preparation by isomerization of the cis-forms.

The bicyclic sulfones (VII) and (III), likewise (X) and (IV), are distinguished between themselves by the configuration at the junction of the rings, but they have the same spatial arrangement of the methyl groups at the second carbon atom. The 2-methylhexahydrothiochromanones (I) and (II) likewise differ from each other only in the arrangement of the methyl groups at the second carbon and are epimers.*

Hence the isomerization of the bicyclic sulfones (VII) and (X) proceeds at the angular hydrogen atom located in the α-position to the carbonyl group, and the previously described [2] isomerization of the thiochromanone (II) and the thiochromanone (I) in presence of sodium methylate is, consequently, an epimerization proceeding under the influence of the sulfide sulfur.

In one of the preceding papers we described the synthesis of the monocyclic unsaturated sulfone (V) and its condensation with butadiene [3]. Hydrogenation of the product of the diene synthesis (VI) under various conditions gives the bicyclic cis-sulfone (VII) or its trans-form (III). Consequently we were unable by this route to obtain the epimeric cis-sulfone (X). This sulfone was synthesized by condensation of butadiene with the unsaturated cyclic sulfone (VIII). The latter was prepared from the saturated sulfone (XI) by bromination followed by cleavage of hydrogen bromide.



Reaction of one molecule of bromine with the sulfone (XI) in glacial acetic acid, in presence of hydrogen bromide as catalyst, at 25-30° gives a mixture of the monobromides (XII) and (XIII) in a total yield of 80%.

When the reaction is performed without catalyst but with heating at 60°, a mixture of the isomeric monobromoketosulfones (XII) and (XIII) is obtained together with a small amount of dibromide in a total yield of up to 80%.

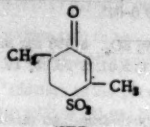
The unsaturated cyclic sulfones (VIII) and (XIV) were prepared by cleavage of hydrogen bromide from the bromoketosulfones (XII) and (XIII) by sodium acetate in boiling acetone.

Heating of sulfone (VIII) with butadiene in dioxan solution in a steel ampoule for 6 hours at 160-200° gave the bicyclic sulfone (IX) in 63% yield.

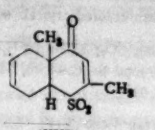
Sulfone (IX) is not isomerized by boiling in a dilute solution of sodium methylate, due to the stabilizing influence of the double bond in the ring. Hydrogenation of the product of the diene condensation (IX) with Pd catalyst in a neutral medium gives the saturated bicyclic cis-sulfone (X) which, as noted above, readily isomerizes to the trans-sulfone (IV) when heated with sodium methylate solution as well as under the action of hydrochloric acid.

* The term "epimers" is applied in the present instance to racemates.

The unsaturated cyclic sulfone (XIV) completely fails to condense with butadiene at 175°, thus behaving like the previously described unsaturated cyclic sulfones (XV), (XVI) and (VI).

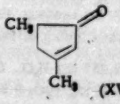


(XV)



(XVI)

(XVII)



(XVIII)

It is known that carbocyclic ketones of similar structure (XVII-XVIII) likewise do not undergo the diene synthesis [4,5]. Consequently substitution in the β-position to the carbonyl group greatly weakens the dienophilic properties of α,β-unsaturated cyclic ketones, just as is the case in the aliphatic series.

EXPERIMENTAL

The starting 2-methyltetrahydro-1-thiopyran-4-one (XI) was prepared by oxidation of 2-methyltetrahydro-1-thiopyran-4-one with potassium permanganate in acetone, as previously described [2,6].

5-Bromo-2-methyltetrahydro-1-thiopyran-4-one oxide (XII) and 3-bromo-2-methyltetrahydro-1-thiopyran-4-one (XIII). a) 5.6 g sulfone (XI) (m.p. 78-79°) was dissolved in 30 ml glacial acetic acid, and to the solution was added 1 ml of 4 N hydrogen bromide in glacial acetic acid. Under energetic stirring for 40 minutes, addition was made of 5.15 g bromine in 10 ml glacial acetic acid. The temperature of the solution was kept at 25-30°. Addition of the whole of the bromine was followed by separation of 4.8 g crystals; partial removal of the acetic acid in vacuum resulted in crystallization of another 1.9 g. In all, 6.7 g of mixed dibromides was obtained, or 80% of the theoretical yield.

4.8 g of the mixture of dibromides was recrystallized from methanol to give 2.4 g of crystals with m.p. 182-184°. Two recrystallizations from methanol gave pure 5-bromo-2-methyltetrahydro-1-thiopyran-4-one (XII) with m.p. 187.5-188°.

9.688 mg substance: 11.127 mg CO_2; 4.238 mg H_2O; 5.833 mg SO_4 + Br. 8.581 mg substance: 9.819 mg CO_2; 3.723 mg H_2O; 5.210 mg SO_4 + Br. Found %: C 31.34, 31.23; H 4.89, 4.85; S 11.04, 10.77; Br 27.49, 26.99. $C_6H_9O_2SBr \cdot 1.5\ CH_3OH$. Calculated %: C 31.15; H 5.23; S 11.09; Br 27.63.

Judging by the analysis, the substance contains methanol of crystallization which is not removed by prolonged drying of the bromide in the vacuum desiccator.

From the mother liquor after distillation of the methanol was separated 2.2 g crystals with m.p. 170-174° which was subjected to hydrogen bromide cleavage without further purification. In this way the unsaturated cyclic sulfone (XIV) was obtained, corresponding to 3-bromo-2-methyltetrahydro-1-thiopyran-4-one dioxide (XIII).

b) 6 g of the starting sulfone (XI) (m.p. 78-79°) was dissolved in 50 ml glacial acetic acid, and to the solution was added 5.5 g bromine. With energetic stirring the solution was heated to 61°. At this temperature instant decolorization of the solution occurred, followed by rapid darkening with temperature rise to 67°. (Further temperature rise was prevented by cooling with ice-water). Fractional crystallization yielded 7 g of crystals of the mixture of dibromides (XII) and (XIII), equivalent to 80% of theory. The first fraction (3 g) was the monobromide (XII), which was followed by a mixture of monobromosulfone and dibromosulfone (m.p. 160-164°). Cleavage of hydrogen bromide from this mixture led to separation of 2-methyl-1-thiopyran-4-one dioxide (V) (m.p. 139-140°), as well as a mixture of the unsaturated sulfones (VIII) and (XIV).

2-Methyl-2,3-dihydro-1-thiopyran-4-one (VIII). 3.2 g of the bromosulfone (XII) (m.p. 187-188°) was dissolved in 60 ml acetone and poured into a suspension of 2 g anhydrous sodium acetate in acetone. With

energetic stirring the mixture was heated for one hour on the water bath at 60-65°. After cooling, the solution was filtered, acidified with strong hydrochloric acid until decolorized, and again filtered. Removal of the solvent by distillation left 1.7 g crude crystals from which was obtained (recrystallization from alcohol) 1.35 g pure sulfone (VIII) in the form of lemon-colored crystals with m.p. 89.5-90°.

6.700 mg substance: 11.031 mg CO_2; 3.035 mg H_2O; 3.995 mg SO_4. 5.598 mg substance: 9.185 mg CO_2; 2.506 mg H_2O; 3.345 mg SO_4. Found %: C 44.93, 44.78; H 5.07, 5.01; S 19.90, 19.95. $C_8H_8O_3S$. Calculated %: C 44.98; H 5.03; S 20.02.

2-Methyl-5,6-dihydro-1-thiopyran-4-one (XIV). 2.2 g of the above-described mixture of bromides (m.p. 170-174°), containing the bromosulfone (XIII), was dissolved in 60 ml acetone, and the solution poured into a suspension of 1.6 g sodium acetate in 60 ml acetone, the mixture being then energetically stirred at 60-65° for one hour. Treatment as above yielded 0.65 g sulfone (XIV) with m.p. 115.6-116° (from alcohol).

5.200 mg substance: 8.580 mg CO_2; 2.257 mg H_2O. 6.798 mg substance: 11.195 mg CO_2; 2.994 mg H_2O. 5.460 mg substance: 9.018 mg CO_2; 2.403 mg H_2O; 3.320 mg SO_4. Found %: C 45.03, 44.94, 45.07; H 4.86, 4.93, 4.92; S 20.29. $C_8H_8O_3S$. Calculated %: C 44.98; H 5.03; S 20.02.

2-Methyl-5,8,9,10-tetrahydro-1-thiochroman-4-one (IX) 1.3 g sulfone (VIII) (m.p. 90°), 3 g butadiene, 15 ml dioxan and 0.01 g pyrogallol were heated in a steel ampoule for 5½ hours at 200°. Removal of the solvent left 1.4 g of condensation product contaminated with polymer. After digestion in alcohol with animal charcoal and three recrystallizations from alcohol, the sulfone (IX) was obtained with m.p. 163-164.5° (yield 63%).

3.410 mg substance: 7.016 mg CO_2; 2.025 mg H_2O. 3.040 mg substance: 6.272 mg CO_2; 1.813 mg H_2O; 1.373 mg SO_4. Found %: C 56.17, 56.20; H 6.64, 6.67; S 15.08. $C_{10}H_{14}O_3S$. Calculated %: C 56.05; H 6.58; S 14.96.

The sulfone (IX) was obtained in a much purer form in an experiment under the same conditions but at 160°.

After boiling in dilute sodium methylate solution in methanol, the sulfone (IX) was recovered unchanged (no melting point depression in admixture with the original sulfone).

2-Methylhexahydro-1-thiochroman-4-one (X). 0.3 g sulfone (IX) (m.p. 163-164°) was hydrogenated with Pd catalyst* in 10 ml acetone. After an hour 35 ml hydrogen (18°, 750 mm) had been absorbed, or one molecule. After removal of solvent the substance melted without recrystallization at 131-132°. Recrystallization from alcohol yielded the cis-form (X) with m.p. 132.5-133°.

6.045 mg substance: 12.277 mg CO_2; 4.035 mg H_2O; 2.683 mg SO_4. 5.045 mg substance: 10.288 mg CO_2; 3.390 mg H_2O; 2.240 mg SO_4. Found %: C 55.42, 55.65; H 7.47, 7.52; S 14.82, 14.82. $C_{10}H_{16}O_3S$. Calculated %: C 55.53; H 7.46; S 14.83.

Isomerization of the cis-sulfone (X) into the trans-sulfone (IV). a) A solution of 0.15 g cis-sulfone (X) (m.p. 132-133°) in 2.5 ml methanol was boiled for 2½ hours. After part distillation of the methanol in vacuum, 70 mg of a substance with m.p. 140-141° separated. After two recrystallizations from alcohol the substance melted at 142.5-143.5° and did not depress the melting point of the previously described trans-sulfone (IV).

b) 0.2 g cis-sulfone (X) (m.p. 132-133°) was dissolved in 5 ml 96% ethyl alcohol and to the solution was added two drops of strong hydrochloric acid. The solvent was evaporated and the resultant crystals were recrystallized from alcohol when they melted at 144-144.5°. No depression of m.p. of the trans-sulfone (IV).

Heating of sulfone (XIV) with butadiene. 0.65 g unsaturated sulfone (XIV) (m.p. 114-115°), 1.5 g butadiene, 7 ml dioxan and 0.02 g pyrogallol were heated in a steel ampoule for 5 hours at 175°. Removal of the solvent left 400 mg substance with m.p. 112-113° (from alcohol). A mixture with the original sulfone melted at 114-115°.

SUMMARY

1. Reaction of one molecule of bromine with a solution of sulfone (XI) in glacial acetic acid gives a mixture of the monobromosulfones (XII) and (XIII) in 80% yield.

* Palladium oxide on calcium carbonate.

2. Heating of the monobromosulfones (XII) and (XIII) with sodium acetate in acetone leads to cleavage of hydrogen bromide with formation of the corresponding unsaturated cyclic sulfones (VIII) and (XIV).

3. Condensation of sulfone (VIII) with butadiene at 160-200° gives the bicyclic sulfone (IX) in 63% yield.

4. Hydrogenation of sulfone (IX) in neutral medium with Pd catalyst yields the saturated bicyclic cis-sulfone (X), an epimer of the previously obtained cis-sulfone (VII).

5. In this manner, in addition to the previously prepared stereoisomeric sulfones (III), (IV), and (VII), a fourth and last stereoisomeric sulfone (X) has been synthesized by the diene condensation.

6. The cis-sulfone (X) readily isomerizes to the trans-form (IV) in presence of sodium methylate.

7. The unsaturated sulfone (XIV), like the previously described sulfones (VI), (XV) and (XVI), does not undergo the diene condensation with butadiene at temperatures up to 200°.

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*See Consultants Bureau translation, p. 1283.
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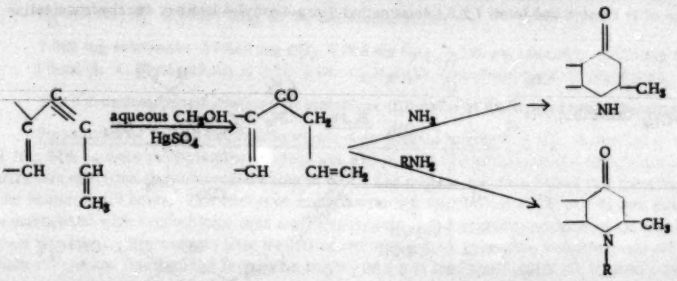
***See Consultants Bureau translation, p. 1045.
****See Consultants Bureau translation, p. 561.
*****See Consultants Bureau translation, p. 1039.

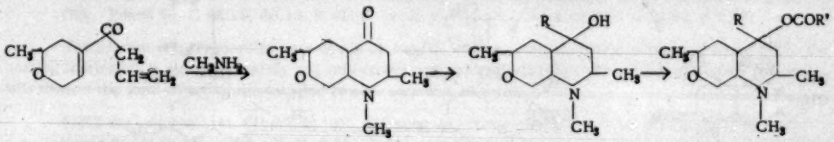
145. HETEROCYCLIC COMPOUNDS. XXI. SYNTHESIS AND TRANSFORMATIONS OF 1,2,6,6-TETRAMETHYL-7-OXA-4-KETODECAHYDROQUINOLINE

I. N. Nazarov and S. A. Vartanyan

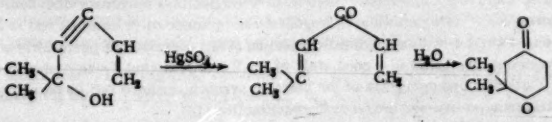
A few years ago we discovered in our laboratory a simple method of preparation of various gamma-piperidones, based upon the hydration of dienynes to the corresponding dienones (vinylallyl ketones) [1] and cyclization of the latter under the action of ammonia and primary amines [2]:



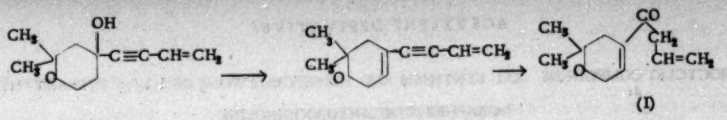
Using this method for preparation of .....γ-piperidones, we recently synthesized 1,2,6-trimethyl-7-oxa-4-decahydroquinoline and obtained a series of the alcohols and esters corresponding thereto [3]:



In the present paper the synthesis is described of two new representatives of the bicyclic pyranopiperidones (II) and (III), starting from 2,2-dimethyltetrahydro-4-pyrone which is easily prepared from the technically available dimethylvinylethinyl carbinol [4]:



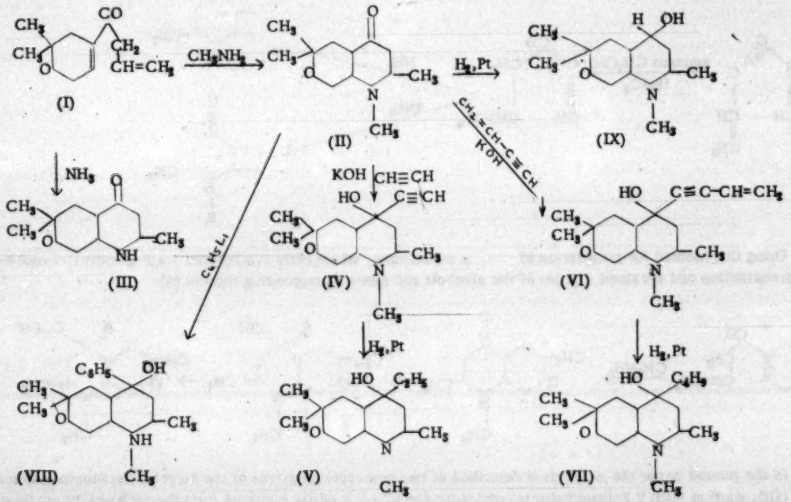
As was shown in an earlier communication, 2,2-dimethyltetrahydro-4-pyrone condenses with vinylacetylene to give 2,2-dimethyl-4-vinylethinyltetrahydro-4-pyranol which dehydrates to the corresponding pyrano diene; hydration of the latter in aqueous methanol solution then results in a high yield of the pyrano dienone (I) [5]:



(I)

Like other vinyallyl ketones, the pyranic dienone (I) readily reacts with ammonia and methylamine to form in good yield, respectively, 2,6,6-trimethyl-7-oxa-4-ketodecahydroquinoline (III) and 1,2,6,6-tetramethyl-7-oxa-4-ketodecahydroquinoline (II).

These compounds are of interest as starting materials for the synthesis of various heterocyclic compounds containing both the piperidine and the tetrahydropyran ring. Under the influences of powdered potassium hydroxide the bicyclic pyranopiperidine (II) readily condenses with acetylene and gives, in a yield of about 70%, 1,2,6,6-tetramethyl-7-oxa-4-ethinyl-4-hydroxy decahydroquinoline (IV), which takes up two molecules of hydrogen when hydrogenated in presence of Pt catalyst and forms 1,2,6,6-tetramethyl-7-oxa-4-ethyl-4-hydroxy-decahydroquinoline (V):



Under the influence of potassium hydroxide the piperidone (II) likewise readily condenses with vinyl-acetylene [6] and gives a good yield of 1,2,6,6-tetramethyl-7-oxa-4-vinylethinyl-4-hydroxy decahydroquinoline (VI) which absorbs three molecules of hydrogen when hydrogenated in presence of Pt catalyst and is converted into 1,2,6,6-tetramethyl-7-oxa-4-butyl-4-hydroxy decahydroquinoline (VII). Reaction of phenyllithium [7] with the bicyclic pyranopiperidone (II) results in a good yield of 1,2,6,6-tetramethyl-7-oxa-4-phenyl-4-hydroxy-decahydroquinoline (VIII). Catalytic hydrogenation of the bicyclic pyranopiperidone (II) in presence of Pt catalyst leads to 1,2,6,6-tetramethyl-7-oxa-4-hydroxydecahydroquinoline (IX).

All of the alcohols of the 7-oxadecahydroquinoline series (IV, V, VI, VII, VIII, and IX) described in this paper were obtained in the form of a mixture of stereoisomers whose separation presents great difficulties, due to the hygroscopicity of the hydrochlorides and their failure to recrystallize. Attempts to prepare esters of these alcohols by acylation with the help of benzoyl chloride, acetyl chloride and propionic anhydride were also unsuccessful. Under mild conditions the hydrochloride of the original piperidol separated in all cases, and under drastic conditions the product resinifies.

EXPERIMENTAL

The starting allyl-2,2-dimethyl-Δ^4-dihydro-4-pyranyl ketone (I) was prepared by the previously described method and had the constants: b.p. 94-96° at 2mm; n_D^{20} 1.4873 [5].

Preparation of 2,6,6-trimethyl-7-oxa-4-ketodecahydroquinoline (III). A mixture of 12 g ketone (I), 100 g aqueous ammonia (s.g. 0.9) and 15 ml methyl alcohol was shaken for 20 minutes until a homogeneous solution was obtained, and then saturated with ammonia at −2° (weight increase 30 g) and heated in a sealed metal cylinder at 80° for 3½ hours. The ammonia was removed in vacuum, at first in the cold and then on a water bath at 45°. The solution was neutralized with hydrochloric acid until weakly acid and the neutral products were extracted with ether, but only a trace was found.

The organic base was salted out with potassium carbonate, extracted with ether, dried with sodium sulfate and distilled in vacuum to give 8.6 g piperidone (III) in the form of a mobile liquid which turned yellow on standing and had a characteristic ammoniacal odor; b.p. 128-130° at 6 mm.

n_D^{20} 1.4911; d_4^{20} 1.0625; MR_D 53.56; calculated 53.90.

7.262 mg substance: 17.850 mg CO_2; 6.350 mg H_2O. 3.595 mg substance: 8.870 mg CO_2; 3.200 mg H_2O. Found %: C 67.08, 67.33; H 9.78, 9.96. $C_{11}H_{19}O_2N$. Calculated %: C 67.00; H 9.64.

The 2,4-dinitrophenylhydrazone of piperidone (III) melts at 210-212° (after recrystallization from alcohol).

Preparation of 1,2,6,6-tetramethyl-7-oxa-4-ketodecahydroquinoline (II). A mixture of 60 g ketone (I) and 70 g 35% aqueous methylamine solution was shaken for a few minutes until a transparent solution was formed (during this operation the temperature rose to 43°). The mixture was then heated in a metallic ampoule at 70° in the course of 1.5 hours. The excess of methylamine was distilled off at 45° in a 75 mm vacuum. The solution was neutralized with hydrochloric acid until weakly acid, and the neutral products extracted with ether, but only a trace was found. The organic base was salted out with sodium hydroxide, extracted with ether, dried with sodium sulfate and fractionated in vacuum to give 58.3 g of piperidone (II) in the form of a liquid which turned yellow on standing and had a characteristic ammoniacal odor; b.p. 113-114° at 2mm.

n_D^{20} 1.4973; d_4^{20} 1.0690; MR_D 59.35; calculated 58.80.

13.48 mg substance: 12.23 mg H_2O; 33.73 mg CO_2. 12.23 mg substance: 11.20 mg H_2O; 30.56 mg CO_2. Found %: C 68.29, 68.19; H 10.15, 10.25. $C_{12}H_{21}O_2N$. Calculated %: C 68.24, H 9.99.

The picrate was prepared by mixing piperidone (II) with saturated alcoholic solution of picric acid. On heating in alcohol it dissolves readily and only comes down after distilling off the greater part of the solvent; it is then in the form of a dark-brown, fine powder with m.p. 162-164°.

5.622 mg substance: 0.616 ml N_2 (24°, 736 mm). 5.920 mg substance: 0.643 ml N_2 (22°, 743 mm). Found %: N 12.33, 12.20. $C_{18}H_{24}O_9N_4$. Calculated %: N 12.72.

Hydrogenation of 1,2,6,6-tetramethyl-7-oxa-4-ketodecahydroquinoline (II). 3.2 g freshly distilled piperidone (II) was hydrogenated in 15 ml ethyl alcohol in presence of Pt catalyst. 360 ml hydrogen was absorbed. Complete hydrogenation of the carbonyl group requires 370 ml hydrogen. Hydrogenation was completed in 2 hours. 1.8 g 1,2,6,6-tetramethyl-7-oxa-4-hydroxydecahydroquinoline (IX) was obtained in the form of a transparent, viscous liquid with a characteristic odor; b.p. 121-122.5° at 2 mm. The product crystallized when petrol (b.p. 45-60°) was added; it was isolated in the form of a white powder with m.p. 131-134°.

12.47 mg substance: 31.08 mg CO_2, 12.19 mg H_2O. 12.28 mg substance: 30.65 mg CO_2; 12.04 mg H_2O. Found %: C 68.02, 68.11; H 10.94, 10.72. $C_{12}H_{23}O_2N$. Calculated %: C 67.60; H 10.80.

The hydrochloride of base (IX) is an amorphous mass which deliquesces on standing in the air.

Synthesis of 1,2,6,6-tetramethyl-7-oxa-4-ethinyl-4-hydroxydecahydroquinoline (IV). Into a three-necked flask fitted with a mechanical stirrer, a dropping funnel and a reflux condenser were introduced 9.4 g powdered potassium hydroxide and 150 ml dry ether. At a temperature of −2° this mixture was saturated with acetylene in the course of 30 minutes. Addition was then made with continuous stirring in a stream of acetylene of 20 g piperidone (IV) dissolved in an equal volume of ether. After the piperidone had been added, the acetylene stream was continued for a further 4 hours at −2° and 2 hours at room temperature. The potassium hydroxide was washed

out with water (10 ml), carbon dioxide was passed through the ether solution for complete removal of the alkali, and the product was dried with sodium sulfate and distilled in vacuum. 16.5 g of the acetylenic alcohol (IV) was obtained in the form of a very viscous, yellow liquid, b.p. 137-139° at 2 mm. It solidified to a vitrous mass in the receiver.

10.53 mg substance: 9.28 mg H_2O; 27.46 mg CO_2. 9.53 mg substance: 8.43 mg H_2O; 24.74 mg CO_2. Found %: C 71.17, 70.85; H 9.87, 9.86. $C_{14}H_{23}O_2N$. Calculated %: C 70.87; H 9.7.

The hydrochloride of the acetylenic alcohol (IV), after drying in a vacuum desiccator over phosphorus pentoxide, melts at 116-120°. It is a hygroscopic, amorphous white powder which deliquesces when stored in contact with air; on recrystallization it comes down in the form of a noncrystalline, amorphous mass.

Hydrogenation of 1,2,6,6-tetramethyl-7-oxa-4-ethinyl-4-hydroxydecahydroquinoline (IV). 3 g of freshly distilled acetylenic alcohol (IV) was hydrogenated in 15 ml alcohol in presence of Pt catalyst, 523 ml hydrogen being absorbed. Complete hydrogenation of the acetylenic alcohol requires 600 ml hydrogen. 2.4 g of 1,2,6,6-tetramethyl-7-oxa-4-ethyl-4-hydroxydecahydroquinoline (V) was obtained in the form of a transparent, viscous liquid with a characteristic odor; b.p. 113-115° at 1 mm.

8.597 mg substance: 21.675 mg CO_2; 8 410 mg H_2O. 4.440 mg substance: 11.215 mg CO_2; 4.350 mg H_2O. Found %: C 68.81, 68.93; H 10 95, 10.96. $C_{14}H_{27}O_2N$. Calculated %: C 69.70; H 11.24.

The hydrochloride of the ethylpiperidol (V) is a viscous mass which does not crystallize.

Synthesis of 1,2,6,6-tetramethyl-7-oxa-4-vinylethinyl-4-hydroxydecahydroquinoline (VI). Into a round-bottomed flask fitted with a mechanical stirrer, a mercury seal and a dropping funnel was introduced 8.4 g powdered potassium hydroxide and 100 ml dry ether. To this mixture, cooled to −2°, was added in small portions with vigorous stirring 10 g vinyl acetylene and 20 g piperidone (II) dissolved in 50 ml dry ether. After the addition of the ether solution of vinylacetylene and piperidone (II), stirring was continued for a further eight hours while being cooled with ice-water, and the reaction mass left overnight. On the next day the mixture was stirred for a further two hours, treated with water (10 ml), and a stream of carbon dioxide passed through the ether layer for complete removal of alkali. The product was then dried with sodium sulfate and distilled in vacuum to give 19.3 g of the vinylacetylenic alcohol (VI); b.p. 150-152° at 1 mm.

15.13 mg substance: 40.37 mg CO_2; 13.06 mg H_2O. 9.63 mg substance: 25.78 mg CO_2; 8.47 mg H_2O. Found %: C 72.83, 73.06; H 9.67, 9.84. $C_{16}H_{25}O_2N$. Calculated %: C 73.01; H 9.58.

This alcohol is a yellowish glassy product which softens on heating. Its hydrochloride is a white hygroscopic powder melting at 120-124°.

Hydrogenation of 1,2,6,6-tetramethyl-7-oxa-4-vinylethinyl-4-hydroxydecahydroquinoline (VI). 3 g freshly distilled material (VI) was hydrogenated in solution in 15 ml alcohol in presence of Pt catalyst. 813 ml hydrogen was absorbed as compared with the theoretical requirement of 822 ml. The catalyst was filtered off, the alcohol distilled off, and the residue fractionated in vacuum to give 2.6 g of the butylpiperidol (VII) as a transparent, viscous liquid with a characteristic odor, b.p. 140-143° (2 mm). This product was a mixture of the two isomers of 1,2,6,6-tetramethyl-7-oxa-4-butyl-4-hydroxydecahydroquinoline. Dilution with ether resulted in crystallization of about 1 g of pure substance which melted at 114-116° (from ether) and was readily soluble in petrol (b.p. 65-78°), acetone and benzene.

4.872 mg substance: 12.742 mg CO_2; 5.105 mg H_2O. 5.673 mg substance: 14.878 mg CO_2; 5.910 mg H_2O. Found %: C 71.37, 71.57; H 11.72, 11.66. $C_{16}H_{31}O_2N$. Calculated %: C 71.37; H 11.52.

The hydrochloride of this alcohol melted at 109-112° after drying in a vacuum desiccator over phosphorous pentoxide. It was a hygroscopic, white amorphous powder which deliquesced in the air and on recrystallization separated in the form of a viscous, noncrystalline mass.

The residue following removal of the crystalline isomer of (VII) was distilled in vacuum to give 1.7 g of a mixture of the isomeric alcohols (VII) with b.p. 140-142° at 2 mm and consisting of a vitreous mass which softened on heating.

4.021 mg substance: 10.480 mg CO_2; 4.120 mg H_2O. 6.005 mg substance: 15.620 mg CO_2; 6.165 mg H_2O. Found %: C 71.13, 70.98; H 11.47, 11.49. $C_{16}H_{31}O_2N$. Calculated %: C 71.37; H 11.52.

The hydrochloride of this mixture melted at 120-123°.

Synthesis of 1,2,6,6-tetramethyl-7-oxa-4-phenyl-4-hydroxydecahydroquinoline (VIII). The following reaction was conducted in a nitrogen atmosphere. Into a three-necked round-bottom flask, fitted with a mechanical stirrer, mercury seal, dropping funnel, a tube for nitrogen and a thermometer, was introduced 50 ml absolute ether, 1 g small lithium turnings and 4 g bromobenzene.

After the reaction had commenced, gradual addition was made of a further 14 g bromobenzene dissolved in the same volume of absolute ether. There was then added to the mixture 50 ml ether, and the reaction mass stirred at room temperature for one hour and then at the temperature of boiling ether for 30 minutes. Dropwise addition was then made at a temperature of −12° to the so-prepared phenyllithium of 9 g of the piperidone (II) dissolved in 10 ml absolute ether. On the following day the mixture was heated for two hours at the temperature of boiling ether, and the reaction product was hydrolyzed with 12 ml of water at a temperature of −6°. The ether layer was separated, and the aqueous layer was extracted with three portions of ether, saturated with potassium carbonate, and extracted once more with ether. The ether extracts were combined, and dried with sodium sulfate, the ether was distilled off, and the product distilled in vacuum giving 9.2 g of the phenylpiperidol (VIII). The latter was a very viscous, yellowish liquid boiling at 163° (1 mm).

4.036 mg substance: 11.092 mg CO_2; 3.340 mg H_2O. 3.995 mg substance: 10.985 mg CO_2, 3.352 mg H_2O. Found %: C 75.00, 75.04; H 9.26, 9.39. $C_{18}H_{27}O_2N$. Calculated %: C 74.74; H 9.3. 0.063 g substance: 4.17 ml CH_4 (19°, 738 mm). 0.080 g substance: 5.3 ml CH_4 (20°, 739 mm). Found %: active hydrogen 0.29, 0.30. Calculated %: active hydrogen 0.34.

On cooling the product solidified to a vitreous mass which was converted by grinding into an amorphous powder. The hydrochloride of this alcohol melted at 185-187° after drying in the vacuum desiccator over phosphorous pentoxide. It behaves like the hydrochloride of the above-described piperidols.

Attempt to prepare the benzoate of 1,2,6,6-tetramethyl-7-oxa-4-phenyl-4-hydroxydecahydroquinoline (XI). To phenyllithium prepared, as described above, from 1 g of small pieces of metallic lithium and 15 g bromobenzene in 50 ml absolute ether was added dropwise 9 g of the piperidone (II) dissolved in the same volume of ether. Mixing was effected for 2 hours at room temperature and 2 hours at the boiling point of ether. There was added to the resultant complex at −5°, dropwise, 10 ml of benzoyl chloride dissolved in 10 ml absolute ether. The mixture was stirred for one hour at 20° and for 3 hours at the boiling point of ether before being left overnight. On the following day there was added 20 ml of water to the reaction mass, the aqueous layer was saturated with sodium carbonate and extracted with ether; the product was dried with sodium sulfate and distilled in vacuum. There was isolated 3.2 g of the above-described phenylpiperidol (VIII) with b.p. 160-164° (1 mm); m.p. of hydrochloride 176-180°. Consequently no benzoylation had taken place under the described conditions.

SUMMARY

Reaction of methylamine and ammonia with the dienone (I) gives, in good yield, the bicyclic γ-piperidones (II and III) containing the condensed tetrahydropyran ring.

Condensation of the bicyclic pyranopiperidone (II) with acetylene and vinylacetylene results in formation in good yield of the acetylenic and vinylacetylenic piperidols (IV and VI).

The phenylpiperidol (VIII) is obtained in good yield by the action of phenyllithium on the bicyclic pyranopiperidone (II).

All the above-described unsaturated compounds were hydrogenated in presence of Pt catalyst to give the corresponding saturated compounds.

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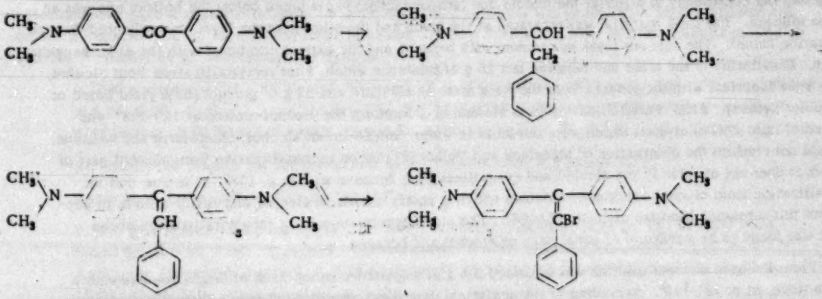
INVESTIGATION OF THE ACTION OF BROMINE ON α,α-(p-DIMETHYLAMINOPHENYL)-β-PHENYLETHYLENE

A. M. Khaletsky and A. M. Yanovitskaya

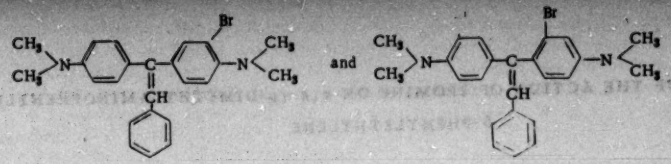
With the objective of studying the action of bromine on triphenylethylene derivatives, we have investigated the behavior of this halogen towards α,α-di-(p-dimethylaminophenyl)-β-phenylethylene. The possibilities arising in the action of bromine on α,α-di-(p-dimethylaminophenyl)-β-phenylethylene are replacement of the hydrogen of the ethylene group by bromine, addition of two atoms of bromine, or substitution of the hydrogen of the benzene ring.

Taking into consideration the stability of the halogen at a double bond, the formation of α,α-di-(p-dimethylaminophenyl)-β-phenyl-β-bromoethylene appeared probable. The synthesis of the latter was of interest in connection with its similarity to triphenylbromoethylene whose estrogenic properties have been described in the literature [1].

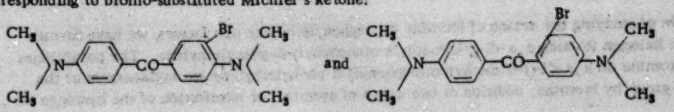
For the synthesis of α,α-di-(p-dimethylaminophenyl)-β-phenyl-β-bromoethylene we started from α,α-di-(p-dimethylaminophenyl)-β-phenylethylene, which was prepared by dehydration of α,α-di-(p-dimethylaminophenyl)-benzyl carbinol. The latter was prepared by the Grignard reaction from Michler's ketone and benzyl chloride:



Reaction of benzyl magnesium chloride with Michler's ketone gave α,α-di-(p-dimethylaminophenyl)-β-phenylethylene together with a small amount of α,α-di-(p-dimethylaminophenyl)-benzyl carbinol, which suggests dehydration of the latter in the course of the reaction. Oxidation of α,α-di-(p-dimethylaminophenyl)-β-phenylethylene with potassium permanganate yielded Michler's ketone; the presence of benzaldehyde was detected by its odor. Bromination of α,α-di-(p-dimethylaminophenyl)-β-phenylethylene with bromine in chloroform led to separation of two products: One of these had a blue color and preponderated; it melted at 151-154°; the other was green and melted at 169-170°. Analysis showed them to be isomers since they both had the composition $C_{24}H_{25}N_2Br$ and contained one atom of bromine. The bromine-containing compounds were oxidized with potassium permanganate (in acetone solution); a substance was obtained which melted at 122-124° and contained halogen; among the oxidation products was benzaldehyde. Since these data clearly indicated that the action of bromine on α,α-di-(p-dimethylaminophenyl)-β-phenylethylene does not result in addition of bromine nor in substitution of hydrogen at the ethylene bond, the only possible conclusion was that bromine replaces hydrogen in the aromatic nucleus. To test this conclusion, Michler's ketone was subjected to bromination when a monobromo derivative with m.p. 118-127° was obtained and was found to be identical with the bromo derivative isolated after oxidation of the bromo-substituted α,α-di-(p-dimethylaminophenyl)-β-phenylethylene. On the basis of these data we can conclude that in the bromination of α,α-di-(p-dimethylaminophenyl)-β-phenylethylene there are formed bromo-substituted derivatives to which the following structure may be attributed:



corresponding to bromo-substituted Michler's ketone:



EXPERIMENTAL

α,α-Di-(p-dimethylaminophenyl)-benzyl carbinol. 53.6 g Michler's ketone, dissolved in benzene, was gradually added to benzyl magnesium chloride in ether. The Grignard reagent was prepared from 4.8 g magnesium and 25.2 g benzyl chloride (b.p. 179°). Heat was developed during the reaction with the ketone. The color of the mixture first turned green and later brown. After the whole of the ketone had been added, the mixture was heated on the water bath with stirring for 3 hours. The reaction product was decomposed with ice-water and acidified with dilute hydrochloric acid until the basic salts of magnesium had gone into solution; three layers were formed. The top one had the consistency of a slurry; the middle one (ether-benzene) had a green color; the bottom one was an aqueous solution. The solid material was separated at the pump and the ether-benzene layer was collected through a separating funnel. The aqueous layer was washed with benzene and the extract combined with the ether-benzene solution. Distillation of the ether and benzene left 25 g of substance which, after recrystallization from alcohol, proved to be identical with the product from the solid mass; in all there was 37 g of product (55% yield based on the Michler ketone). After recrystallization from alcohol or chloroform the product melted at 127-128° and consisted of light-yellow crystals which were insoluble in water, soluble in hot alcohol, chloroform and benzene. We could not confirm the observation of Madelung and Volker [2] that on recrystallization from alcohol part of the product does not dissolve in the alcohol and crystallizes from benzene with m.p. 173°. It is true that on recrystallization from alcohol a residue is obtained which is poorly soluble in alcohol and easily soluble in benzene, but this substance likewise melts at 127-128°. The most appropriate solvent for crystallization of the product was found to be a mixture of equal parts of alcohol and benzene.

From the acid aqueous solution was separated 2.5 g of a substance in the form of bright needles with a greenish tinge, m.p. 187-189°. According to the analytical data these corresponded to α,α-di(p-dimethylaminophenyl)-benzyl carbinol. The product melting at 127-128° appeared, judging by the analysis, to be α, α-di-(p-dimethylaminophenyl)-β-phenylethylene.

In general the obtained results are consistent with those of other workers [3] who brought Michler's ketone into reaction with various organomagnesium compounds and obtained not tertiary alcohols but products of their dehydration. Attention may be drawn to the fact that it is more expedient to use a deficiency of ketone in relation to the benzyl chloride (not more than 60% of the theoretical) since it is rather difficult to eliminate unreacted ketone.

Analysis of α,α-di-(p-dimethylaminophenyl)-benzyl carbinol.

0.1186 g substance: 7.60 ml N_2 (21°, 768 mm). 0.0988 g substance: 6.60 ml N_2 (18°, 745 mm). Found %: N 7.51, 7.69. $C_{24}H_{28}ON_2$. Calculated %: N 8.77.

Analysis of α,α-di-(p-dimethylaminophenyl)-β-phenylethylene.

0.0902 g substance: 6.20 ml N_2 (20°, 776 mm). 0.0824 g substance: 5.70 ml N_2 (19°, 774 mm). Found %: N 8.11, 8.19. $C_{24}H_{26}N_2$. Calculated %: N 8.18.

Oxidation of α,α-di-(p-dimethylaminophenyl)-β-phenylethylene. 3.42 g α,α-di-(p-dimethylaminophenyl)-

β-phenylethylene was dissolved in 50 ml acetone and oxidized with 126.4 ml 1% potassium permanganate solution for 2 hours with stirring. After distillation of the acetone, the residue was filtered, washed with hot water and treated with hot benzene. The benzene was driven off to leave 1.6 g of a greenish substance, melting (after recrystallization from alcohol) at 170-172° and not depressing the melting point of Michler's ketone. The aqueous liquid had a strong odor of benzaldehyde. The formation of Michler's ketone and benzaldehyde on oxidation demonstrates that the compound has the structure of α,α-di-(p-dimethylaminophenyl)-β-phenylethylene.

Bromination of α,α-di-(p-dimethylaminophenyl)-β-phenylethylene. 171.1 g α,α-di-(p-dimethylaminophenyl)-β-phenylethylene was dissolved in 85 ml chloroform, and to the solution, with stirring, was gradually added a solution of 8 g bromine in 25 ml chloroform. Heat was developed during this addition and the color changed from light-green to blue with a greenish tinge. After removing the chloroform, there remained a viscous, blue mass which slowly crystallized. On recrystallization from alcohol it was found to be heterogeneous; the greater part had a blue color and melted at 151-154°; its amount was 14.2 g; a subsequent series of recrystallizations from benzene yielded 5.1 g substance with m.p. 169-170°; the color of this was light-green. The total yield was thus 19.3 g or 68% of theory.

Analysis of the bromide with m.p. 151-154°.

0.1496 g substance: 8.60 ml N_2 (18°, 760 mm). 0.1783 g substance: 10.20 ml N_2 (17°, 770 mm). 0.4700 g substance: 10.75 ml 0.1 N $AgNO_3$ (by Stepanov's method). 0.4372 g substance: 10.10 ml 0.1 N $AgNO_3$. Found %: N 6.74, 6.81; Br 18.24, 18.47. $C_{24}H_{25}N_2Br$. Calculated%: N 6.65; Br 19.00

Oxidation of the bromide melting at 151-154°. 4.2 g of the bromide was dissolved in 50 ml acetone and the solution oxidized with 126 ml of 1% solution of potassium permanganate. The precipitate formed after driving off the acetone was filtered and washed with hot water; the aqueous liquid had the odor of benzaldehyde and gave a negative reaction for bromine. The precipitate was worked up with hot benzene and ether. After distilling off the solvents there remained a yellow mass which after recrystallization melted at 122-124°. Yield 2.04 g. No reaction for halogen.

0.1098 g substance: 7.8 ml N_2 (16°, 770 mm). 0.1248 g substance: 8.7 ml N_2 (18°, 772 mm). Found %: N 8.50, 8.28. $C_{17}H_{19}ON_2Br$. Calculated %: N 8.04. 0.2007 g substance: 5.05 ml 0.1 N $AgNO_3$. 0.2218 g substance: 5.95 ml 0.1 N $AgNO_3$. Found %: Br 20.12, 21.42. $C_{17}H_{19}ON_2Br$. Calculated %: Br 23.00.

An attempt to prepare the semicarbazone of the bromo ketone was unsuccessful.

Analysis of the bromide with m.p. 169-170°.

0.1495 g substance: 8.80 ml N_2 (18°, 770 mm). 0.1620 g substance: 9.40 ml N_2 (18°, 766 mm). Found %: N 6.99, 6.86. $C_{24}H_{25}N_2Br$. Calculated %: N 6.65. 0.4824 g substance: 11.00 ml 0.1 N $AgNO_3$ (by Stepanov's method). 0.4538 g substance: 10.80 ml 0.1 N $AgNO_3$. Found %: Br 18.26, 19.02. $C_{24}H_{25}N_2Br$. Calculated %: Br 19.00.

Oxidation of the bromide with m.p. 169-170°. This was effected, as above, with 1% potassium permanganate solution. The bromo ketone had a yellow color, somewhat paler than previously, and melted after recrystallization from benzene at 166-167°. The aqueous alkaline liquid gave off the odor of benzaldehyde and gave a negative reaction for bromine. The following results were obtained in nitrogen determinations (Dumas) and bromine determinations (Pirn and Schiff):

0.1194 g substance: 7.80 ml N_2 (15°, 770 mm). 0.0807 g substance: 5.30 ml N_2 (16°, 770 mm). 0.2090 g substance: 5.80 ml 0.1N $AgNO_3$. 0.2326 g substance: 6.70 ml 0.1 N $AgNO_3$. Found %: N 7.84, 7.86; Br 22.12, 23.02. $C_{17}H_{19}ON_2Br$. Calculated %: N 8.04; Br 23.00.

An attempt to prepare the semicarbazone of the bromo ketone was unsuccessful.

Bromination of Michler's ketone. 2.68 g Michler's ketone was dissolved in 50 ml chloroform, and to the solution was gradually added a solution of 1.6 g bromine in 15 ml chloroform. After driving off the chloroform and recrystallizing from alcohol and benzene there was obtained 2.5 g of a substance with a gradual melting point of 117-128°; it was evidently a mixture of the isomeric monobromo derivatives of the ketone whose separation was attended with difficulties.

SUMMARY

1. Reaction of benzyl magnesium chloride with Michler's ketone gives mainly α,α-di-(p-dimethylaminophenyl)-β-phenylethylene together with a smaller amount of α,α-di-(p-dimethylaminophenyl)-benzyl carbinol.

2. In the reaction of bromine with α,α-di-(p-dimethylaminophenyl)-β-phenylethylene the bromine replaces a hydrogen of the aromatic nucleus with formation of isomeric bromo derivatives of α,α-di-(p-dimethylaminophenyl)-β-phenylethylene.

3. A monobromo-substituted ketone is formed by the action of bromine on Michler's ketone

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SYNTHESIS OF 3,4-BENZPHENANTHRENE AND ITS HOMOLOGS

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3,4-Benzphenanthrene is the simplest aromatic hydrocarbon possessing a specific carcinogenic activity; the isomeric tetracyclic hydrocarbons, chrysene and 1,2-benzanthracene do not exhibit such activity, although the nucleus of the latter is also present in molecules which are more strongly carcinogenic. Certain homologs of 3,4-benzphenanthrene also possess carcinogenic activity, and this fact has attracted the attention of chemists to hydrocarbons of the benzphenanthrene series and has stimulated the search for methods for their synthesis.

A few methods are known for the preparation of benzphenanthrene homologs. Of the methods related to the Pschorr synthesis the most satisfactory was found to be that proposed by Hewett [1], based on cyclization with the aid of potassium hydroxide into quinolines halogenated in one of the aromatic nuclei of α,β-diarylacrylic acids; investigation of the biological properties of compounds obtained by this route provided fundamental material for the problem of the relation between the carcinogenic properties and the structure of hydrocarbons of this series.

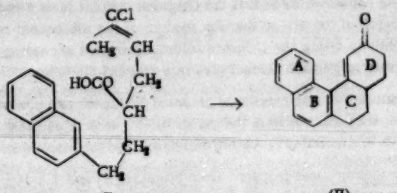
Successful use was also made of some variants of syntheses utilizing intramolecular acylation of γ-aryl butyric acids [2]. Starting materials for these syntheses are compounds of the phenanthrene series in whose molecules is an additional ring. The butyric acid residue necessary for this ring-closure is usually attached to the initial phenanthrene derivative with the help of the classical Reformatsky reaction.

Less suitable methods are those based on the application of the diene synthesis; the yields of adducts in such cases are generally very small. The most promising of the methods of this group is the synthesis based on addition of maleic anhydride to homologs of 1-phenyl-3,4-dihydronaphthalene [3].

It must furthermore be noted that due to the difficult accessibility of the starting substances and the numerous steps in the syntheses, and also due in some cases to the low yields, the hydrocarbons of the 3,4-benzphenanthrene series are even today not readily accessible. The difficulty of preparing compounds of this series has been frequently mentioned in the literature [4].

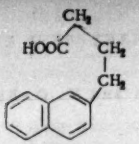
It has been shown [5] that polycyclic ketones and hydrocarbons can be synthesized with the help of sulfuric acid hydrolysis of unsaturated compounds containing a halogen atom at the double bond; on treatment with sulfuric acid, α-(3-chlorocrotyl)-γ-aryl butyric acids undergo hydrolysis and twofold cyclization with formation of polycyclic ketones which can be converted into the corresponding hydrocarbons.

A similar transformation of α-(3-chlorocrotyl)-γ-(2-naphthyl)-butyric acid (I) should lead to ketone (II) containing the 3,4-benzphenanthrene skeleton:



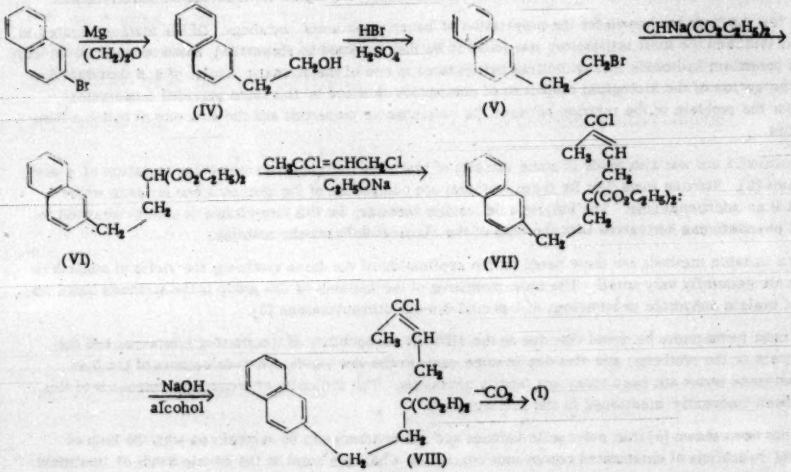
(I) (II)

It would appear that in this case closure of ring C could proceed completely or partially also in another direction with formation of a ketone containing the 1,2-benzanthracene skeleton. However, the literature on the cyclization of γ-(2-naphthyl)-butyric acids not substituted in the side chain suggests that this possibility can be excluded; in all cases when γ-(2-naphthyl)-butyric acid (III) does not contain a substituent in the 8-position, the ring closes at position 1, and the product is a compound of the penanthrene series.



(III)

Use may therefore be made, as starting material for synthesis of compounds of the benzphenanthrene series, of α-(3-chlorocrotyl)-γ-(2-naphthyl)-butyric acid (I), which was obtained according to the scheme below.



The reaction of ethylene oxide with the magnesium derivative of 2-bromonaphthalene was investigated for the first time by Sontage [6] who obtained from 153 g of bromo compound a total of 13 g of impure β-(2-naphthyl)-ethyl alcohol (IV). Karrer and co-workers [7], however, succeeded in obtaining this alcohol by the same route in a yield of 45% of theory. This difference in yields and the poor reproducibility of the experiments were explained by Yu. S. Zalkind [8] who showed that the Grignard reagent from 2-bromonaphthalene is extraordinarily easily oxidized by oxygen of the air, so that the product of the subsequent reaction will always contain a considerable amount of β-naphthol. Using the Grignard solution prepared according to Yu. S Zalkind's instructions in a hydrogen stream, we were able to prepare alcohol (IV) in a yield of 69-70%.

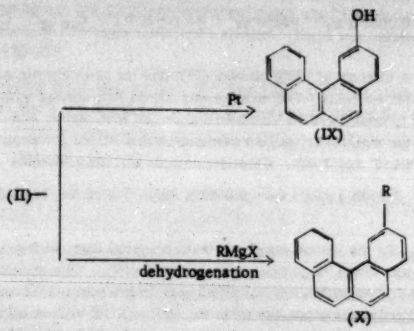
β-(2-Naphthyl)-ethyl bromide (V) was previously prepared by Karrer and coworkers [7] by reacting alcohol (IV) with phosphorous tribromide; they did not state the yield. It was ascertained that bromide (V) may be prepared in 82% yield by boiling a mixture of alcohol (IV) with hydrobromic and sulfuric acids.

Acid (I), as shown in the scheme, was prepared from bromide (V) and 1,3-dichlorobutene-2 by the malonic synthesis. Hydrolysis and double cyclization of acid (I) was effected with the help of sulfuric acid of s.g. 1.78 at 45-55° in a carbon dioxide atmosphere. As was to be expected, the product of cyclization was 6-keto-6,7,8,8a,9,10-hexahydro-3,4-benzphenanthrene (II), which was formed in 69% yield.

Attempts to dehydrogenate this ketone with selenium and sulfur were unsuccessful; with selenium a resin was formed from which it was impossible to isolate a pure substance; with sulfur a crystalline product was obtained which contained sulfur and was not further examined.

On dehydrogenation, however, with platinum black as well as with palladium black, and after removal

of small amounts of neutral products from the dehydrogenated material, there was obtained 6-hydroxy-3,4-benzphenanthrene (IX) in 78% yield. By distillation with zinc dust, this substance was reduced to 3,4-benzphenanthrene which was identified through the picrate. The yield of benzphenanthrene was 50% of the theoretical.



The presence of the carbonyl group provided the possibility of passage from ketone (II) to homologs of benzphenanthrene containing substituents in the 6-position. Since, however, ketone (II) is an α,β-unsaturated ketone another possibility was addition of Grignard reagent at the 1,4-position with formation of saturated ketones substituted at the angular carbon atom 4b. In that case dehydrogenation of the reaction products would be accompanied by cleavage of alkyl groups from the quaternary carbon atom to give 3,4-benzphenanthrene or its 6-hydroxy derivative as end-product. In the present case, however, this course of the reaction would be improbable because addition of an alkyl group to the carbon atom 4b would be sterically hindered.

Dehydrogenation of the product of reaction of ketone (II) with excess of methyl magnesium iodide gave the 6-methyl-3,4-benzphenanthrene previously described by Hewett [1] and it was identified through the picrate. Thus the Grignard reagent had added on at the carbonyl group of the ketone. Similarly, by the action on the ketone of the Grignard reagents prepared from ethyl bromide and bromobenzene there were obtained 6-ethyl- and 6-phenyl-3,4-benzphenanthrenes, not previously described in the literature. These hydrocarbons were obtained in yields of 62-84%.

The 6-methyl homolog, like other monomethyl benzphenanthrenes, is carcinogenically active [9]. In view of the fact that, contrary to expectations, the 9-methyl-10-ethyl-1,2-benzanthracene synthesized by Mikhailov and Chernova [10] did not surpass 9,10-dimethyl benzanthracene in activity [11], it is also of interest to investigate the biological properties of 6-ethyl and 6-phenyl benzphenanthrenes.

EXPERIMENTAL

The initial 2-bromonaphthalene was prepared by the method of Newman and Wise: Thermal decomposition of a mixture of the dry double salt of naphthyl diazonium chloride with mercuric bromide and sodium bromide.

β-(2-Naphthyl)-ethyl alcohol (IV). Into a mixture of 11.4 g active magnesium and a small amount of dry ether was poured a few milliliters of a solution of 100 g 2-bromonaphthalene in 400 ml absolute ether; the mixture was heated to boiling on the water bath and to it was added 2 ml Grignard solution prepared from a mixture of ethyl chloride and 2-bromonaphthalene. After the reaction had started, addition was made to the reaction mixture over a short period of all the remaining 2-bromonaphthalene solution. The reaction was performed at the boil and with continuous passage of a slow stream of dry hydrogen. From time to time the mixture was stirred mechanically. The reaction was substantially completed after 3 hours when 0.5-0.8 g magnesium remained in the flask. The solution was cooled in a freezing mixture and gradual addition was made, with intensive mechanical stirring, of an excess (20-25 g) of ethylene oxide in absolute ether. The thickened mass was left overnight and then boiled on the water bath for 2 hours. The ice-cooled reaction mixture was decomposed with dilute hydrochloric acid and the contents of the flask were then subjected to steam-distillation with the aim of removing unreacted bromonaphthalene and the naphthalene formed by decomposition of the Grignard reagent. Steam-distillation was continued until there was substantially no precipitation of crystalline material on the walls of the condenser. The

organic substance remaining in the flask solidified on cooling and was dissolved in ether; the ether solution was washed with weak alkali and then water before drying with sodium sulfate. The residue after driving off the ether was distilled in vacuum. At 180-184° and 15 mm, 58 g (69.8% of theory) distilled over as a light-yellow liquid which crystallized completely in the receiver. After recrystallization from petroleum ether the colorless crystals melted at 67-68°.

0.1032 g substance: 0.3184 g CO_2; 0.0666 g H_2O. Found %: C 84.14; H 7.17. $C_{12}H_{12}O$. Calculated %: C 83.7; H 6.99.

β-(2-Naphthyl)-ethyl bromide (V). A mixture of 108 g alcohol (IV), 250 ml hydrobromic acid (s.g. 1.52) and 50 ml conc. sulfuric acid was refluxed for 4-5 hours. The mixture was cooled and diluted with water when the bromide crystallized; this was dissolved in ether, washed with alkali and then with water, and dried with sodium sulfate. After driving off the ether the residual crystalline substance was distilled in vacuum when 121.2 g bromide (82% of theory) came over at 138-140° and 3 mm. Colorless crystals with m.p. 64-65°.

0.1123 g substance: 0.0893 g AgBr. 0.1152 g substance: 0.0922 g AgBr. Found %: Br 33.84, 34.05. $C_{12}H_{11}Br$. Calculated %: Br 34.0%.

β-(2-Naphthyl)-ethyl malonate (VI). To the sodium ethyl malonate prepared from 14.2 g sodium, 170 g absolute alcohol and 100 g ethyl malonate was added 92 g of crystalline bromide (V). The mixture was boiled for 5 hours. After cooling, the mixture was diluted with water, acidified with hydrochloric acid until weakly acid, the straw-colored liquid product was dissolved in ether, the ether solution washed with water and dried with sodium sulfate. After the solvent had been driven off, the product distilled at 198° and 3 mm. 80.05 g (65.25% of theory) of ester (VI) was obtained.

d_4^{20} 1.0976; n_D^{20} 1.5420.

0.1110 g substance: 0.2260 g CO_2; 0.0732 g H_2O. Found %: C 72.72; H 7.32. $C_{19}H_{22}O_4$. Calculated %: C 72.61; H 7.0.

[β-(2-Naphthyl)-ethyl-(3-chloro)-crotyl]-malonate (VII). To a solution of sodium alcoholate prepared from 4.4 g sodium and 50 ml absolute alcohol was added 59 g of the monosubstituted malonate (VI). The mixture was heated on the water bath for 30 min., after which it was cooled to room temperature. Gradual addition was then made of 30 g freshly distilled 1,3-dichlorobutene-2. The mixture was refluxed for 5 hours, then cooled, and addition made of dilute hydrochloric acid in amount sufficient to dissolve the formed salt. The product was extracted with ether, the ether solution washed with water and dried with sodium sulfate. After driving off the ether, the product distilled at 230-231° at 3mm, giving 61.9 g (81.8% of theory) of the disubstituted malonate (VII) as a viscous, light-yellow liquid.

d_4^{20} 1.123; n_D^{20} 1.5460.

0.1134 g substance: 0.0413 g AgCl. 0.1132 g substance: 0.0414 g AgCl. Found %: Cl 9.01, 9.05. $C_{23}H_{27}O_4Cl$. Calculated %: Cl 8.81.

[β-(2-Naphthyl)-ethyl-(3-chloro)crotyl]-malonic acid (VIII). A mixture of 90 g ester (VII), 27.2 g sodium hydroxide and 380 g 90% alcohol was boiled on the water bath for 4 hours, following which 150 ml water was added and the alcohol completely distilled off. The solution was acidified with hydrochloric acid when a heavy oil separated. The substance was dissolved in ether, washed with water and dried with sodium sulfate. The crystalline substance remaining after removal of the ether was washed with benzene. There was obtained 56 g (70% of theory) of colorless, thin crystals with m.p. 167°.

0.1128 g substance: 0.0490 g AgCl. 0.1072 g substance: 0.0458 g AgCl. Found %: Cl 10.75, 10.57. $C_{19}H_{19}O_4Cl$. Calculated %: Cl 10.25.

α-(3-Chlorocrotyl)-γ-(2-naphthyl)-butyric acid (I). 10 g of the pure dibasic acid (VII) was decomposed by heating over the naked flame. The resultant thick oil was distilled at 234-235° at 4 mm, giving 8.3 g (95% of theory) of a light-yellow, viscous oil.

d_4^{20} 1.1568; n_D^{20} 1.5848.

0.1143 g substance: 0.0510 g AgCl. 0.1291 g substance: 0.0630 g AgCl. Found %: Cl 12.10, 12.08. $C_{18}H_{19}O_2Cl$. Calculated %: Cl 11.73.

6-Keto-6,7,8,8a,9,10-hexahydro-3,4-benzphenanthrene (II). To 70 g of 84.5% sulfuric acid was added 7 g acid (I). After standing for a short period at room temperature, the mixture was heated on the water bath at 45-55° in a stream of carbon dioxide for 30 min. The heating was attended with copious evolution of hydrochloric acid. After the substance had completely gone into solution and the evolution of hydrochloric acid had ceased, the dark-red solution was left overnight at room temperature. On the following day the contents of the flask were poured on to ice, the resultant grey precipitate was filtered, carefully washed with dilute alkali and then with water, dried, and recrystallized from alcohol. There was obtained 4 g (69.68% of theory) of colorless crystals with m.p. 125-126°.

0.1203 g substance: 0.3830 g CO_2; 0.0733 g H_2O. 0.1120 g substance: 0.357 g CO_2; 0.0672 g H_2O. Found %: C 86.82, 86.93; H 6.07, 6.66. $C_{18}H_{16}O$. Calculated %: C 87.09; H 6.45.

The 2,4-dinitrophenylhydrazone was prepared in an alcoholic medium and recrystallized from chloroform. Red crystals, m.p. 173-174°.

0.1005 g substance: 12 ml N_2 (22°, 683 mm). 0.0715 g substance: 8.8 ml N_2 (27°, 680 mm). Found %: N 12.43, 12.52. $C_{24}H_{20}N_4O_4$. Calculated %: N 13.00.

Dehydrogenation of ketone (II) with sulfur. A mixture of 1 g ketone (II) and 0.3 g powdered sulfur was heated at 210° for 30 minutes until no more hydrogen sulfide came off, and the contents of the flask were transferred to a porcelain beaker and thoroughly triturated with dilute alkali, then filtered and washed with water. The substance retained on the filter was dissolved in alcohol; the alcoholic solution was digested with active carbon, filtered, and diluted with water. The resultant light-yellow acicular crystals melted at 172-173°. The product contained sulfur.

0.1024 g substance: 0.056 g $BaSO_4$. 0.1109 g substance: 0.059 g $BaSO_4$. Found %: S 7.56, 7.30.

6-Hydroxy-3,4-benzphenanthrene (IX). A mixture of 0.8 g catalyst (palladium on carbon, 5% metal content) and 2 g ketone (II) was heated in a carbon dioxide stream at 300-320° for 1 hour. The product was extracted with benzene, the solution filtered off, treated with dilute alkali solution and dried. After removal of the benzene there was not a large amount of neutral dehydrogenation products. Acidification of the alkaline solution led to separation of a viscous oil which was dissolved in ether. After removal of the ether, the residue was dissolved in alcohol and the alcoholic solution digested with active carbon. Dilution of the filtered solution with water brought down white, fluffy crystals in an amount of 1.55 g (78.8% of theory). M.p. of the colorless crystals 108-110°.

0.1034 g substance: 0.3350 g CO_2; 0.049 g H_2O. Found %: C 88.35; H 5.26. $C_{18}H_{12}O$. Calculated %: C 88.52;; H 4.91.

The dark-red picrate, recrystallized from alcohol, had m.p. 147-148°.

0.0728 g substance: 6.2 ml N_2 (21°, 680 mm). Found %: N 8.85. $C_{24}H_{15}N_3O_8$. Calculated %: N 8.88.

3,4-Benzphenanthrene. A homogeneous mixture of 1.5 g 6-hydroxy-3,4-benzphenanthrene and 12 g zinc dust was heated in a quartz test tube to dark-red heat and the heating continued until no more viscous, dark oil separated. The product was dissolved in ether, the solution was washed with alkali and then with water and dried with sodium sulfate. The oil remaining after removal of the ether was rubbed with a small amount of alcohol, when it crystallized. The alcoholic solution of the substance was digested with active carbon, and the greater part of the solvent was driven off from the filtered solution. A precipitate of colorless acicular crystals was formed in quantity of 0.7 g (50% of theory, m.p. 67-68°.

0.1023 g substance: 0.3557 g CO_2; 0.0536 g H_2O. Found %: C 94.82; H 5.82. $C_{18}H_{12}$. Calculated %: C 94.73; H 5.27.

The picrate had a brick-red color and melted at 126° (from alcohol).

0.0986 g substance: 9.1 ml N_2 (23°, 677 mm). 0.0940 g substance: 8.6 ml N_2 (23°, 677 mm). Found %: N 9.33, 9.47. $C_{24}H_{15}N_3O_7$. Calculated %: N 9.20.

6-Methyl-, 6-ethyl- and 6-phenyl-3,4-benzphenanthrenes (X). These hydrocarbons were prepared in the following manner: To a Grignard reagent prepared from a 3- to 4-fold molar excess of the corresponding alkyl (aryl) halide was added 6-10 g ketone (II); the mixture was boiled on the water bath for 2 hours and left overnight.

While cooling with ice-water, the reaction mixture was decomposed by addition of water and dilute hydrochloric acid, the product was extracted with ether, and the ethereal solution was washed and dried. Removal of the ether left a viscous oil which was dehydrogenated with platinum black (approximately 0.1 g black per 1 g substance) at 300-320° for about 30 min. The product was extracted with benzene, the benzene solution was filtered from catalyst, and the benzene removed. Phenyl benzphenanthrene was obtained in the crystalline form after removal of the benzene. The methyl and ethyl benzphenanthrenes were distilled in vacuum. The ethyl derivative crystallized in the receiver during the distillation, but the methyl compound was only obtained in the crystalline form after conversion of the vitreous product into the picrate, recrystallization of the picrate from methyl alcohol and decomposition with aqueous ammonia. The hydrocarbons, likewise the picrates, were purified by recrystallization from ethyl alcohol, with the exception of the picrate of phenyl benzphenanthrene which was purified with the help of benzene since it decomposed into its constituents when treated with alcohol.

In the table are shown the properties and yields of the hydrocarbons and their picrates, also the analytical data.

R-	B.p.	M.p.	Yield (in % of theory)	Analysis				M.p. of picrate	Analysis of picrate	
				Found %		Calculated %			Found %	Calcd. %
				C	H	C	H		N	N
CH_3	206-208° (2 mm)	80-81°	76.92	94.06	5.94	94.21	5.78	–	–	–
C_2H_5	215-218 (2.5 mm)	82-83	62	93.88	6.54	94.75	6.25	104-105°	8.93	8.66
C_6H_5	–	127-128	84.35	94.77	5.72	94.73	5.47	107-108	8.17	7.88

SUMMARY

It is shown that under the action of sulfuric acid, α-(3-chlorocrotyl)- γ-(2-naphthyl)butyric acid undergoes hydrolysis and double cyclization to form 6-keto-6,7,8,8a,9,10-hexahydro-3,4-benzphenanthrene. Dehydrogenation of this ketone gave 3,4-benzphenanthrene in 50% yield.

The above α,β-unsaturated ketone adds on alkyl magnesium halides at the double bond of the carbonyl group. 6-Methyl-, 6-ethyl- and 6-phenyl-3,4-benzphenanthrenes were synthesized by dehydrogenation of the products of reaction of the ketone with the corresponding Grignard reagents.

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ALKANE SULFONIC ACIDS

IV. REACTIONS OF ALKANESULFOCHLORIDES WITH BENZIDINE

A. G. Kostsova

The objective of this investigation was the study of the reaction of alkane sulfochlorides with a more complex amine, namely, the bicyclic-diamine benzidine [1]. This reaction could proceed according to one of the schemes below or according to the two schemes concurrently:

1. $RSO_2Cl + NH_2C_6H_4{\cdot}C_6H_4NH_2 = RSO_2NHC_6H_4{\cdot}C_6H_4NH_2 + HCl$;
2. $2RSO_2Cl + NH_2C_6H_4{\cdot}C_6H_4NH_2 = RSO_2NHC_6H_4{\cdot}C_6H_4NHSO_2R + 2HCl$,

i.e. in the first case a mono-(alkanesulfo)-benzidide could be formed and in the other a di-(alkanesulfo)-benzidide.

We proceeded to investigate this reaction, also the effect of the conditions, particularly solvents and temperatures. The reaction was performed by heating to 70° and also at room temperature, using alcohol or pyridine as reaction media. Examination of the reaction products revealed that in all cases di-(alkanesulfo)-benzidide is formed, and, as a rule, benzidine hydrochloride is obtained as a secondary product. Thus the reaction proceeds according to the scheme:

$$2RSO_2Cl + 2NH_2C_6H_4{\cdot}C_6H_4NH_2 = RSO_2NHC_6H_4{\cdot}C_6H_4NHSO_2R + HCl{\cdot}NH_2C_6H_4{\cdot}C_6H_4NH_2{\cdot}HCl.$$

We reacted methane-, ethane- and butanesulfochlorides with benzidine. The reaction products were grey-pink, amorphous powders, melting above 200° with decomposition, very difficultly soluble in the majority of solvents. In the cold they dissolve fairly readily in pyridine, and when heated they partially dissolve in alcohol. They dissolve in alkali from which they are brought down by acidification with dilute sulfuric or hydrochloric acid. This property was exploited in separating them from by-products.

EXPERIMENTAL

1. Reaction of methanesulfochloride with benzidine in a pyridine medium. To 2.4 g benzidine dissolved in 10 ml pyridine was gradually added 1.5 g methanesulfochloride. The temperature rose to 70-75° and a dark-red precipitate came down. The reaction mixture was left for 24 hours at room temperature, and the precipitate then collected and dried. Examination of the solubility of the precipitate in water revealed that a portion was readily soluble and went into solution, while a portion remains undissolved, thus demonstrating the heterogeneity of the crude product. Two methods were used for separating the components.

a) Half of the crude product was treated with boiling water, a portion going into solution. A grey-white crystalline substance came down from the solution on cooling, and was identified, through the nitrogen determination, as benzidine hydrochloride.

0.1057 g substance: 8.12 ml 0.1 N H_2SO_4. Found %: N 10.74. $C_{12}H_{14}N_2Cl_2$. Calculated %: N 10.89.

The water-insoluble portion was found to contain nitrogen and sulfur but no halogen. The analytical data are consistent with it being the basic reaction product, di-(methanesulfo)-benzidide with the structure $CH_3SO_2NHC_6H_4{-}C_6H_4NHSO_2CH_3$.

0.1240 g substance: 7.13 ml 0.1 N. H_2SO_4. Found %: N 8.05. $C_{14}H_{16}O_4N_2S_2$. Calculated %: N 8.23.

The product was purified by dissolving in pyridine and precipitating with water. It melts above 200° with decomposition.

b) Our second method of separating the reaction product from benzidine hydrochloride was based on the solubility in alkali and on the separation of the product when the alkaline solution was acidified. The second half of the crude product was dissolved in 5% alkali; the undissolved residue was filtered off and the alkaline filtrate acidified with 5% sulfuric acid until the turbidity did not disappear. After standing for a short

period with cooling, a pinkish amorphous product came down and was filtered, washed with water and dried. In its properties it resembled the product isolated in the aqueous treatment, as was confirmed by analysis. The over-all yield of the product isolated by both methods was 50% of the theoretical. The same product is formed by heating on a water bath under a reflux condenser for one hour, i.e. di-(methanesulfo)-benzidide.

2. Reaction of methanesulfochloride with benzidine in alcohol. 2.7 g benzidine was dissolved in 30 ml absolute alcohol by heating on the water bath. To the solution, cooled to room temperature, was added 1.6 g methane sulfochloride in small portions. A light-pink precipitate came down and, after collection, was separated into its components by the above-described method. The total yield of di-(methanesulfo)-benzidide was 59%. The same product is obtained in 70% yield by refluxing on the water bath under the same conditions in an alcoholic medium. Consequently, in all the conditions employed by us, one and the same products are formed: di-(methanesulfo)-benzidide and (as by-product) benzidine hydrochloride.

3. Reaction of ethanesulfochloride with benzidine in pyridine. 3 g benzidine, 12 ml pyridine and 2.1 g ethanesulfochloride were taken. The reaction course and the separation of products were conducted as above. The properties of the isolated di-(ethanesulfo)-benzidide resembled those of di-(methanesulfo)-benzidide. It melts above 200° with decomposition. It was recrystallized from pyridine and water. Yield 50% of theory. Reaction in pyridine with heating gives a 58% yield of di-(ethanesulfo)-benzidide.

0.1500 g substance; 7.99 ml 0.1 N H_2SO_4. Found %: N 7.45. $C_{16}H_{20}O_4N_2S_2$. Calculated %: N 7.60.

4. Reaction of ethanesulfochloride with benzidine in alcohol. 4.6 g benzidine was mixed with 40 ml absolute alcohol and 3.2 g ethanesulfochloride. Further procedure was as above. Yield 72% of the theoretical. Reaction in alcohol with heating gave 78% yield. Regardless, therefore, of our experimental conditions, ethanesulfochloride gives di-(ethanesulfo)-benzidide as the main product and benzidine hydrochloride as by-product.

5. Reaction of butane sulfochloride with benzidine in alcohol. 2.9 g benzidine, 25 ml absolute alcohol and 2.5 g butanesulfochloride were taken. Further treatment was as above. Yield of di-(butanesulfo)-benzidide 60%; its crystalline structure was more strongly defined and it was more easily soluble in alcohol than the above-described methane- and ethanesulfobenzidides. It likewise melts above 200° with decomposition.

0.0892 g substance: 3.85 ml 0.1 N H_2SO_4. Found %: N 6.04. $C_{28}H_{36}O_4N_2S_2$. Calculated %: N 6.60.

SUMMARY

1. Di-(methanesulfo)-, di-(ethanesulfo)- and di-(butanesulfo)-benzidides have been prepared and characterized.

2. It is shown that the reaction proceeds in one direction regardless of the conditions, namely, with formation of di-(alkanesulfo)-benzidide and benzidine hydrochloride.

3. The reaction is shown to proceed more completely in an alcoholic medium when heated.

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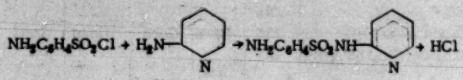
ALKANESULFONIC ACIDS

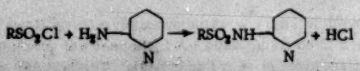
V. REACTION OF ALKANESULFOCHLORIDES WITH α-AMINOPYRIDINE AND SULFANILAMIDE

A. G. Kostsova

The purpose of the investigation was the study of the reaction of alkanesulfochlorides with α-aminopyridine and sulfanilamide. One of the most important derivatives of α-aminopyridine in the aromatic series is sulfidine, in which the sulfanilic acid residue is linked to the α-aminopyridine residue. The reaction is represented by the following equation:

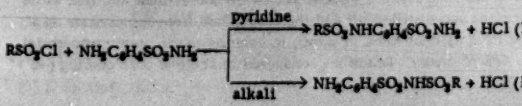


We wished to perform the reaction with alkanesulfochlorides according to the above scheme:



We see from the above equations that the product which we had in view must be similar in structure to sulfidine, but differs from the latter in containing an aliphatic radical in place of the $NH_2C_6H_4$ group characteristic of sulfidine. Since our investigations are largely concerned with the interaction of alkanesulfochlorides with aromatic amines [1], it was of interest also to study the reaction with α-aminopyridine with methane-, ethane-, 2-methylethane-, butane-, 2-methylpropane- and 2-methylbutanesulfochlorides. Experiments showed that the reactions proceed best of all in benzene at room temperature. The products are alkane sulfo-α-aminopyridides (main products) and a yellow, heavy oil which appears to be a mixture of unreacted α-aminppyridine and its hydrochloride. 2-Methylethane-sulfochloride is somewhat exceptional in that it forms, under these conditions, a negligible amount of 2-methylethane sulfo-α-aminopyridide, whereas when the reaction is performed in acetone with heating the results are entirely satisfactory. The reaction product — 2-methylethane sulfo-α-aminopyridide — also differs from the derivatives of the other sulfochlorides in being readily soluble in water in the cold, whereas all the others only dissolve in water when boiled and come down again on cooling. Its melting point is much higher in comparison with the other members of the series. These differences are evidently the consequence of structural features of 2-methylethylsulfo-α-aminopyridide in which the sulfamidine group is attached to the secondary carbon whereas in the other compounds it is at a primary carbon.

The reaction of alkanesulfochlorides with sulfanilamide has been described in the literature [2,3]. The reaction was performed in pyridine and in an alkaline medium. It was shown that its course varies with the medium. Thus in pyridine, N^4-alkanesulfosulfanilamide is formed, and in alkali N^1-alkanesulfosulfanilamide, which may be represented by the following scheme:



We conducted the reaction between alkanesulfochlorides and sulfanilamide in an acetone medium with heating on the water bath under a reflux condenser. The constants and the properties of the compounds which we prepared show that under our experimental conditions N^4-alkanesulfosulfanilamides are formed, i.e. the reaction proceeds according to variant (I) in the above scheme.

Sulfanilamide was reacted with methane-, ethane- and 2-methylpropanesulfochlorides. The table lists the compounds prepared, their melting points and their solubilities.

Compounds	Formulas	M.p.	Solubility				
			Water	Alcohol	Alkali	Acetone	Benzene
Methanesulfo-α-aminopyridide	$CH_3SO_2NHC_5H_4N$	194°	Poor	Poor	Good	Good	Good
Ethanesulfo-α-aminopyridide	$CH_3CH_2SO_2NHC_5H_4N$	163					
2-Methylethanesulfo-α-amino pyridide	$(CH_3)_2CHSO_2NHC_5H_4N$	203	Good	Poor	Good	Poor	Poor
Butanesulfo-α-aminopyridide	$CH_3CH_2CH_2CH_2SO_2NHC_5H_4N$	97	Poor	Poor	Good	Good	Good
2-Methylpropanesulfo-α-amino-pyridide	$(CH_3)_2CHCH_2SO_2NHC_5H_4N$	103					
2-Methylbutanesulfo-α-amino-pyridide	$(CH_3)_2CHCH_2CH_2SO_2NHC_5H_4N$	108					
N^4-Methanesulfoanilamide	$CH_3SO_2NHC_6H_4SO_2NH_2$	181	Poor	Good	Good	Good	Good
N^4-Ethanesulfosulfanilamide	$CH_3CH_2SO_2NHC_6H_4SO_2NH_2$	176					
N^4-2-Methylpropanesulfosulfanilamide	$(CH_3)_2CHCH_2SO_2NHC_6H_4SO_2NH_2$	151					

EXPERIMENTAL

1. Preparation of methanesulfo-α-aminopyridide. 4.9 g α-aminopyridine (recrystallized from petroleum ether) and 3 g methanesulfochloride were dissolved in 40 ml benzene. A little heat was developed during mixing. A reddish-brown oil settled to the bottom of the flask together with fine crystals. The benzene was evaporated. The mixture of oil and crystals was treated with cold alcohol which dissolved the oil but not the crystals. The latter were filtered off and the oil solution distilled. The alcohol was driven off on the water bath and the residue distilled in vacuum (b.p. 106° at 20 mm). Only a negligible amount came over under these conditions and rapidly crystallized. The greater part of the oil decomposed. The crystalline product melted at 55°. A nitrogen determination showed this to be unreacted α-aminopyridine. The part of the oil which decomposed during distillation was apparently a mixture of α-aminopyridine hydrochloride and α-aminopyridine. The fine crystals were dried and recrystallized from water (or acetone). Yield 35% of the theoretical.

0.042 g substance: 4.85 ml 0.1 N H_2SO_4. Found %: N 16.16. $C_6H_8O_2N_2S$. Calculated %: N 16.27.

2. Preparation of ethanesulfo-α-aminopyridide. 2.9 g α-aminopyridine and 2 g ethanesulfochloride were dissolved in 40 ml benzene. In this case a crystalline product was not precipitated at once. The benzene solution, separated from the oil, was evaporated in a porcelain beaker; with progressive evaporation of the benzene the sides of the beaker became more and more covered with white crystals of ethanesulfo-α-aminopyridide. It was recrystallized from water. Yield 45% of the theoretical.

0.1035 g substance: 11.3 ml 0.1 N H_2SO_4. Found %: N 15.28. $C_7H_{10}O_2N_2S$. Calculated %: N 15.05.

3. Preparation of 2-methylethanesulfo-α-aminopyridide.* In this case the acetone was used as reaction medium because in benzene the yields are negligible. 2,4 g α-aminopyridine was dissolved in 15 ml anhydrous acetone and dropwise addition was made of 2 g 2-methylethanesulfochloride. Slight heat was developed. The reaction was completed by heating on the water bath. A layer of viscous yellow oil was formed and fine white crystals settled out at the same time. The acetone was distilled off and the oil drained from the crystals on a Schott filter. The crystals were recrystallized from alcohol since in water, in contrast to the previous material, they were readily soluble in the cold. Yield 40% of theory. Reactions conducted in acetone with cooling (+2°) and at room temperature gave yields of 35-37%.

0.1181 g substance: 11.73 ml 0.1 N H_2SO_4. 0.0950 g substance: 0.1083 g $BaSO_4$. Found %: N 13.90; S 15.63. $C_8H_{12}O_2N_2S$. Calculated %: N 13.99; S 16.02.

4. Preparation of butanesulfo-α-aminopyridide. 2.8 g α-aminopyridine and 2.3 g butanesulfochloride were dissolved in 30 ml benzene. Further treatment was as for the preparation of methane- and ethanesulfo-α-aminopyridides. The crystals were separated from the oil, washed with alcohol, and recrystallized from water.

*Compound prepared and characterized by O.I.Strepetova.

Needles. Yield 32% of theory.

0.0924 g substance: 8.19 ml 0.1 N H_2SO_4. Found %: N 12.40. $C_9H_{14}O_2N_2S$. Calculated %: N 13.08.

5. Preparation of 2-methylpropanesulfo-α-aminopyridide. 2.4 g α-aminopyridine and 2 g 2-methylpropanesulfochloride were dissolved in 40 ml benzene. The crystals remaining after evaporation of the benzene were well-formed prisms. Recrystallized from water. Yield 30% of theory.

0.0812 g substance: 7.38 ml 0.1 N H_2SO_4. Found %: N 12.72. $C_9H_{14}O_2N_2S$. Calculated %: N 13.08.

6. Preparation of 2-methylbutanesulfo-α-aminopyridide.* 2.2 g α-aminopyridine and 2 g 2-methylbutanesulfochloride were dissolved in 40 ml benzene. The reaction products were isolated as before. Yield 48% of theoretical. When the reaction in benzene was carried out with application of heat, the yield fell to 11% and the amount of oil sharply increased. Reaction in ice resulted in a yield of about 34%.

0.1142 g substance: 10 ml 0.1 N H_2SO_4. 0.1720 g substance: 0.1780 g $BaSO_4$. Found %: N 12.26; S 14.19. $C_{10}H_{16}O_2N_2S$. Calculated %: N 12.28; S 14.03.

The oil isolated in all these reactions behaves similarly, i.e. on distillation a small amount of α-aminopyridine comes over while the main bulk decomposes. Its composition has consequently not been finally established.

The prepared alkanesulfo-α-aminopyridides are fairly stable to hydrolysis. Thus, for example, when they are boiled in water, alkali and acid and then cooled, they are quantitatively recovered unchanged. In the case of the alkaline solution, the products only come down after acidification with a strictly equivalent amount of acid. If an excess of acid is used, the product again goes into solution because a salt is apparently formed at the expense of the hetero atom of the pyridine ring.

7. Preparation of N^4-methanesulfosulfanilamide. A mixture of 4 g sulfanilamide, 1.7 g methanesulfochloride and 25 ml acetone was refluxed on the water bath for 3 hours. At the end of the reaction the precipitated sulfanilamide hydrochloride was separated and the acetone solution was evaporated. The residue was recrystallized from aqueous alcohol. Yield 83% of the theoretical.

0.060 g substance: 4.73 ml 0.1 N H_2SO_4. Found %: N 11.03. $C_7H_{10}O_4N_2S_2$. Calculated %: N 11.20.

8. Preparation of N^4-ethanesulfosulfanilamide. 2 g ethanesulfochloride and 5 g sulfanilamide were taken in 25 ml acetone. Further procedure as above. Yield 52% of the theoretical.

0.1638 g substance: 12.61 ml 0.1 N H_2SO_4. Found %: N 10.77. $C_8H_{12}O_4N_2S_2$. Calculated %: N 10.60.

9. Preparation of N^4-2-methylpropanesulfosulfanilamide. 2 g 2-methylpropanesulfochloride and 2.3 g sulfanilamide were reacted in 20 ml acetone. Separation and purification of product were carried out as above.

0.0930 g substance: 6.35 ml 0.1 N H_2SO_4. Found %: N 9.55. $C_{10}H_{16}O_4N_2S_2$. Calculated %: N 9.58.

SUMMARY

1. Methane-, ethane-, 2-methylethane-, 2-methylpropane-, butane- and 2-methylbutanesulfo-α-aminopyridides have been prepared for the first time and characterized.

2. The exceptional behavior of 2-methylethanesulfochloride in its reaction with α-aminopyridine is shown in relation to solvents and in relation to the properties of the resultant 2-methylethanesulfo-α-aminopyridide.

3. N^4-Methane, N^4-ethane- and N^4-2-methylpropanesulfosulfanilamides have been prepared and characterized.

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* Compound prepared and characterized by V. I. Sergeeva.

** See Consultants Bureau translation, p. 307.

ALKANESULFONIC ACIDS

VI. REACTIONS OF ALKANESULFOCHLORIDES WITH ANILINE AND p-ANISIDINE

A. G. Kostsova

As we have already pointed out in previous communications [1], N-substituted amides of alkanesulfonic acids have only recently been the subject of investigation. Some of them were prepared in our laboratory. These include acyl amides, anilides, p-toluidides, phenetidides, α- and β-naphthylamino derivatives of chloromethane- and α-chloroethanesulfonic acids.

Among other Russian researches in this field reference may be made to the work of Melnikov [2] which occupies a rather special place in the sense that we have in view chiefly N-alkyl- and aryl-substituted amides, whereas this author prepared a whole series of N-dichloramides of alkanesulfonic acids possessing high germicidal activity. Incidentally we may say that all the N-dichloramides of chloromethanesulfonic acids described by Melnikov were prepared by us (as that author also notes) as far back as 1935 [3].

Interest in the alkanesulfonic acids and their derivatives grows each year since the sulfonic acids and their diverse derivatives (acid chlorides, amides, N-substituted amides, esters, etc.) have found practical application in various branches of the chemical industry [4]. Our present investigation concerns N-aryl amides of unsubstituted alkanesulfonic acids. Of these the p-toluidides and the p-phenetidides have been fairly closely described in the literature [5]. We considered it of interest to perform the reaction of alkanesulfochlorides with aniline and p-anisidine. The reaction of alkanesulfochlorides with aniline has been inadequately studied. There are short notes in the literature on the anilide of methanesulfonic acid and certain other anilides [6]. We have prepared and described the anilides of chloromethane- and α-chloroethanesulfonic acids [1]. In the present investigation we have prepared the anilides of methane-, ethane-, 2-methylethane-, 2-methylpropane- and 2-methylbutanesulfonic acids. The reaction was carried out in ether as the medium, using one equivalent of sulfochloride to two equivalents of aniline in accordance with the equation:

$$RSO_2Cl + 2C_6H_5NH_2 = RSO_2NHC_6H_5 + C_6H_5NH_2 \cdot HCl.$$

The prepared amides present a twofold interest: 1) They are interesting for the problem of the effect of substituents in the benzene ring upon the properties of the compounds; 2) the reaction of anilide formation can be applied to separation of primary and secondary amines as has been done with aromatic sulfochlorides [7]. Separation is based on the ability of primary amines to form products with sulfochlorides which are soluble in alkalis, while secondary amines give products which are insoluble in alkalis.

We are the first to have carried out the reactions of alkanesulfochlorides with p-anisidine. The reactions proceed according to the above scheme. They were carried out under the same conditions as for aniline. We have prepared ethane- and 2-methylethanephenetidides. The first of these is mentioned in the literature [5]. Latimer and Bost obtained it by reacting ethanesulfochloride with p-phenetidine in a pyridine medium. We repeated the preparation in an ethereal medium. The second was prepared by us for the first time. We prepared the anilides and p-anisidides of methane-, ethane-, 2-methylethane-, 2-methylpropane-, 2-methylbutanesulfonic acids and the p-phenetidides of ethane- and 2-methylethanesulfonic acids, whose properties are set out in Tables 1 and 2.

We see from these tables that all the compounds are crystalline and have well-defined melting points which can be used for identification of alkanesulfonic acids. It is noteworthy that the melting points of derivatives of 2-methylethanesulfonic acid are much higher than those of neighboring members of the series. Evidently the effect of the location of the sulfamide group at the secondary carbon is here manifested. These tables also show that the introduction of alkoxyl groups (CH_3O, C_2H_5O) into the aromatic nucleus of anilides usually raises the melting point. The good solubility of these compounds in alkalis was utilized for their separation from the reaction mixture; they were subsequently precipitated by acid from the alkaline solution. We recrystallized the

reaction products from hot water or by dissolving them in a little alcohol and precipitating with water.

TABLE 1

Anilides of alkanesulfonic acids

Name of compounds	Formula	M.p.	Solubility				
			Water	Alkali	Benzene	Ether	Alcohol
Methanesulfanilide	$CH_3SO_2NHC_6H_5$	96°	Poor	Good	Good	Good	Good
Ethanesulfanilide	$CH_3CH_2SO_2NHC_6H_5$	55					
2-Methylethanesulfanilide	$(CH_3)_2CHSO_2NHC_6H_5$	84					
2-Methylpropanesulfanilide	$(CH_3)_2CHCH_2SO_2NHC_6H_5$	37					
2-Methylbutanesulfanilide	$(CH_3)_2CHCH_2CH_2SO_2NHC_6H_5$	42					

TABLE 2

p-Anisidides and p-phenetidides of alkanesulfonic acids

Name of compounds	Formula	M.p.	Solubility				
			Water	Alkali	Benzene	Ether	Alcohol
Methanesulfanisidide	$CH_3SO_2NHC_6H_4OCH_3$	114°	Poor	Good	Good	Good	Good
Ethanesulfanisidide	$CH_3CH_2SO_2NHC_6H_4OCH_3$	63					
2-Methylethanesulfanisidide	$(CH_3)_2CHSO_2NHC_6H_4OCH_3$	78					
2-Methylpropanesulfanisidide	$(CH_3)_2CHCH_2SO_2NHC_6H_4OCH_3$	45					
2-Methylbutanesulfanisidide	$(CH_3)_2CHCH_2SO_2NHC_6H_4OCH_3$	56					
Ethanesulfophenetidide	$CH_3CH_2SO_2NHC_6H_4OC_2H_5$	80					
2-Methylethanesulfophenetidide	$(CH_3)_2CHSO_2NHC_6H_4OC_2H_5$	95					

EXPERIMENTAL*

The starting sulfochlorides were prepared as described in preceding communications [1].** The aniline and the p-phenetidine were freshly distilled; the p-anisidine was recrystallized from water.

1. Preparation of methanesulfanilide. 2 g methanesulfochloride, 3.2 g aniline and 30 ml absolute ether were refluxed on the water bath. At the end of the reaction the precipitated aniline salt was separated; the ethereal filtrate was either evaporated or the ether was distilled off. The residue was dissolved in dilute alkali (5%) and precipitated with dilute sulfuric acid. Yield 40% of the theoretical.

0.0650 g substance. 3.8 ml 0.1 N H_2SO_4. 0.0989 g substance: 0.1365 g $BaSO_4$. Found %: N 8.18; S 18.92. $C_7H_9O_2NS$. Calculated %: N 8.18; S 18.71.

2. Preparation of ethanesulfanilide. 4.35 g ethanesulfochloride and 6.3 g aniline were reacted in 40 ml ether. The product was separated and purified as above. Yield 65% of the theoretical.

0.0800 g substance: 4.24 ml 0.1 N H_2SO_4. 0.090 g substance: 0.1134 g $BaSO_4$. Found %: N 7.42; S 17.28. $C_8H_{11}O_2NS$. Calculated %: N 7.56; S 17.29.

3. Preparation of 2-methylethanesulfanilide. 2 g 2-methylethanesulfochloride and 2.6 g aniline were reacted in 25 ml ether. Further procedure as above. Yield 53% of the theoretical. Reaction in ether at room temperature gives the same product in 50% yield. Reaction in benzene with heating gives a yield of 57%, without heating a yield of 43%. Reaction without a solvent gives a yield of 64-65%. In the latter case a mixture of two crystalline products is formed: aniline salt and 2-methylethanesulfanilide. The mixture was fractionated either by extraction with ether (in which the salt is poorly soluble) or by direct recrystallization from water (both products dissolve in hot water but only the reaction product comes down on cooling). Two recrystallizations lead to a perfectly pure product.

0.1296 g substance: 6.44 ml 0.1 N H_2SO_4. 0.1263 g substance: 0.1466 g $BaSO_4$. Found %: N 6.95; S 15.91. $C_9H_{13}O_2NS$. Calculated %: N 7.03; S 16.08.

* Strepetova and Sergeeva participated in the experimental work.

** 2-Methylethanesulfochloride was prepared by this method for the first time.

4. Preparation of 2-methylpropanesulfanilide. 4 g 2-methylpropanesulfochloride was reacted with 4.6 g aniline in 20 ml ether. Procedure as above. When the crude reaction product was dissolved in alkali and then precipitated with acid, a crystalline product did not separate but a yellow oil came down which could only be crystallized by very intense cooling and prolonged rubbing with a glass rod. Yield 35% of the theoretical.

0.0980 g substance: 4.5 ml 0.1 N H_2SO_4. 0.1102 g substance: 0.1195 g $BaSO_4$. Found %: N 6.42; S 14.86. $C_{10}H_{15}O_2NS$. Calculated %: N 6.57; S 15.02.

5. Preparation of 2-methylbutanesulfanilide. 2 g 2-methylbutanesulfochloride and 1.8 g aniline were reacted in 40 ml ether. Yield 45% of the theoretical. Reaction without heating in ether gives a yield of 37-38%; in benzene with heating the yield is 34%, without heating it is negligible.

0.0553 g substance: 2.38 ml 0.1 N H_2SO_4. 0.1469 g substance: 0.1500 g $BaSO_4$. Found %: N 6.02; S 14.00. $C_{11}H_{17}O_2NS$. Calculated %: N 6.16; S 14.09.

6. Preparation of methanesulfanisidide. 1.86 g methanesulfochloride and 3 g p-anisidine were reacted in 40 ml ether. The reaction was effected as with aniline. Yield of product 30% of the theoretical.

0.0480 g substance: 2.20 ml 0.1 N H_2SO_4. 0.0891 g substance: 0.1025 g $BaSO_4$. Found %: N 6.41; S 15.77. $C_8H_{11}O_3NS$. Calculated %: N 6.96; S 15.92.

7. Preparation of ethanesulfanisidide. 2 g ethanesulfochloride and 3.8 g p-anisidine were reacted in 40 ml ether. Yield 72% of the theoretical. Reaction in ether at room temperature gives approximately the same yield; in benzene at 60° the yield is 60%, without heating 49%.

0.1390 g substance: 6.50 ml 0.1 N H_2SO_4. 0.1201 g substance: 0.1286 g $BaSO_4$. Found %: N 6.54; S 14.68. $C_9H_{13}O_3NS$. Calculated %: N 6.51; S 14.88.

8. Preparation of 2-methylethanesulfanisidide. 2 g 2-methylethanesulfochloride was reacted with 3.38 g p-anisidine in 40 ml ether. Yield 64% of the theoretical; without heating in ether the yield is 57%. In benzene the yield with heating is 45%. Without a solvent the yield is 37-38%.

0.1223 g substance: 5.31 ml 0.1 N H_2SO_4. 0.1484 g substance: 0.1498 g $BaSO_4$. Found %: N 6.07; S 13.84. $C_{10}H_{15}O_3NS$. Calculated %: N 6.11; S 13.97.

9. Preparation of 2-methylpropanesulfanisidide. 2 g 2-methylpropanesulfochloride and 2.3 g p-anisidine were reacted in 40 ml ether. Yield 30% of the theoretical. Approximately the same yield in ether without heating.

0.0880 g substance: 3.40 ml 0.1 N H_2SO_4. 0.0992 g substance: 0.0960 g $BaSO_4$. Found %: N 5.40; S 13.26. $C_{11}H_{17}O_3NS$. Calculated %: N 5.76; S 13.16.

10. Preparation of 2-methylbutanesulfanisidide. 2 g 2-methylbutanesulfochloride was reacted with 2.8 g p-anisidine in 40 ml ether. With heating the yield of product was 68-69%, without heating 46-47%.

0.0598 g substance: 2.32 ml 0.1 N H_2SO_4. 0.1354 g substance: 0.1221 g $BaSO_4$. Found %: N 5.43; S 12.36. $C_{12}H_{19}O_3NS$. Calculated %: N 5.44; S 12.45.

11. Preparation of ethanesulfophenetidide. 2 g ethanesulfochloride was reacted with 4.2 g p-phenetidine in 40 ml ether. Yield 80% of the theoretical

0.1036 g substance: 4.56 ml 0.1 N H_2SO_4. Found %: N 6.16. $C_{10}H_{15}O_3NS$. Calculated %: N 6.11.

The sulfur was not determined in this compound.

12. Preparation of 2-methylethanesulfophenetidide. 1.42 g 2-methylethanesulfochloride and 2.74 g p-phenetidine were reacted in 40 ml ether. With heating the yield was 75% of the theoretical, without heating 53-54%. In benzene with heating the yield was 49.5%, without heating 45.5%; without a solvent the yield was 65.8%.

0.1209 g substance: 4.93 ml 0.1 N H_2SO_4. 0.1644 g substance: 0.1581 g $BaSO_4$. Found %: N 5.70; S 13.18. $C_{11}H_{17}O_3NS$. Calculated %: N 5.76; S 13.16.

All the compounds prepared were fairly resistant to hydrolysis. They were recovered unchanged after boiling for 10-15 minutes with water, dilute alkali and dilute acid.

SUMMARY

1. Reactions of alkanesulfochlorides with aniline, p-anisidine and p-phenetidine have been studied.

2. Preparation and characterization were carried out of the anilides, and p-anisidides of methane-, ethane-, 2-methylpropane-, and 2-methylbutanesulfonic acids, and of the p-phenetidides of ethane- and 2-methylethanesulfonic acids.

3. The reactions of alkanesulfochlorides with amines can be applied to the separation of primary and secondary amines.

4. The preparation of anilides, anisidides and phenetidides can be utilized for identification of alkanesulfonic acids.

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HYDROXYFUCHSONE DYES

XVI [1]. 2-HYDROXYFUCHSONE

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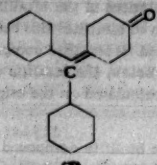
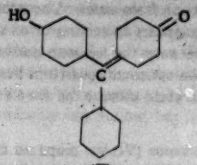
Of the hydroxy derivatives of fuchsone (I) only benzaurin (II) [2] and aurin (III) [2], containing hydroxyl groups in the p-positions of one or both benzene rings of the fuchsone complex, have been at all closely investigated.



(I)



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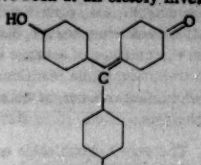
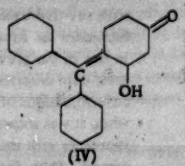


(III)

It has been established that the various properties of hydroxyfuchsone dyes, their color [4], stability of their hydrochlorides [5], their relations with corresponding carbinol derivatives [5], etc. depend on the number of hydroxyl groups. With the aim of investigating the influence of the position of the hydroxyl groups, we decided to compare benzaurin (II) with the isomeric 2-hydroxyfuchsone (IV) which contain the hydroxyl group not at a benzene nucleus but at the quinoid nucleus of the fuchsone complex:



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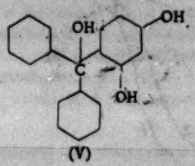
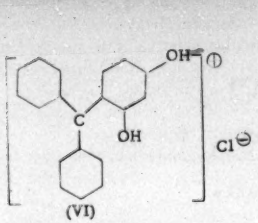


(V)

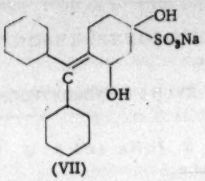
The corresponding carbinol derivative, 2,4-dihydroxytriphenylcarbinol (V), has already been described by Bayer [6] who prepared it by condensing phenyl magnesium bromide with 2,4-dihydroxybenzophenone. By this route, however, the yield of carbinol (V) is very low, and great difficulties are met with in the separation and purification of this compound. We applied the method of condensation of benzophenone chloride with resorcinol to the preparation of 2-hydroxyfuchsone and its corresponding carbinol. This general method of preparation, proposed by Gomberg and Jickling [7], was applied and somewhat improved in our laboratory [8] for the preparation of both fuchsone itself and 3-methoxyfuchsone.

Qualitative experiments showed that the condensation of benzophenone chloride with resorcinol proceeds very rapidly, much more rapidly than with phenol or guaiacol. In view, however, of the high melting point of resorcinol, the condensation is better conducted in an organic solvent, the most suitable being glacial acetic acid. By this means not only is the condensation of benzophenone chloride with resorcinol itself speeded up but the isolation is facilitated of the condensation product which generally has a low stability and decomposes when heated. For the latter reason a low reaction temperature is also preferable. The color changes to crimson during the process due to the formation of 2-hydroxyfuchsone hydrochloride, an onium salt with structure (VI): (see top of next page).

As was confirmed by further experiments with an existing pure preparation, this salt readily hydrolyzes, and when heated it decomposes to form benzophenone; in order to isolate it from the reaction mass, we therefore used a method based on preparation of the bisulfite derivative, which had been successfully used in our laboratory [8] for the preparation of fuchsone and 3-methoxyfuchsone.



(VI)



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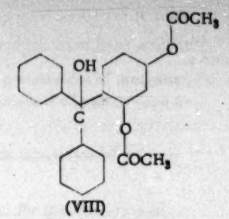
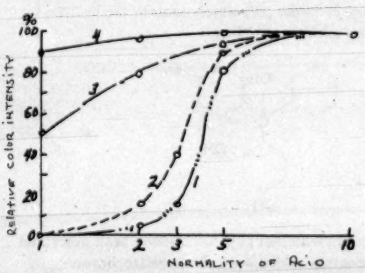


(VIII)

The bisulfite compound, to which on the basis of previous studies [9] we ascribe the structure (VII), is obtained by direct treatment of the reaction mixture with an aqueous solution of sodium bisulfite. It forms colorless crystals, easily purified by crystallization from water. The aqueous solutions of the bisulfite derivative turn yellow when heated, but the color disappears on cooling or on addition of bisulfite; this behavior suggests the presence of a labile equilibrium between the fuchsone derivative and its bisulfite compound. By careful treatment of the reaction mass under the optimum conditions described below, the bisulfite derivative of 2-hydroxyfuchsone can be obtained pure in a yield close to the theoretical, calculated on the original chlorobenzophenone.

The pure hydrochloride of 2-hydroxyfuchsone (VI) was prepared from the bisulfite compound by the action of hydrochloric acid. It is a crystalline powder with a red color, melting (in a rapid melting point determination) at 105-107°. Even at 80-85°, however, the color begins to darken and hydrochloric acid is evolved, indicating dissociation of the hydrochloride. This dissociation also proceeds, although very much slower, when the preparation is kept in an open vessel at room temperature.



Colorimetric evaluation of the degree of hydrolysis of salts of fuchsone (1), 2-hydroxyfuchsone (2), benzaurin (3), and aurin (4) in hydrochloric acid solutions of various strengths.

The stability of 2-hydroxyfuchsone hydrochloride is also very low in aqueous solutions, the latter undergoing hydrolysis with relative ease. Salts of other hydroxyfuchsones are much more resistant to hydrolysis. In one of the previous communications [5] results were described of comparative colorimetric determinations of various hydroxyfuchsones when it was shown that resistance to hydrolysis increases with increasing number of hydroxyl groups. Thus, for example, in 1 N hydrochloric acid the salt of aurin is only hydrolyzed to the extent of 10%, that of benzaurin to the extent of 50%, while fuchsone (containing no hydroxyl groups) is nearly completely hydrolyzed. It was found, however, that resistance to hydrolysis depends not only on the number of hydroxyl groups but also on their position. The salt of 2-hydroxyfuchsone, isomeric with benzaurin but containing the hydroxyl group not at the benzene ring but at the quinoid ring, resembles not the salt of benzaurin but that of fuchsone (which does not contain a hydroxyl group) in its ease of hydrolysis, being hydrolyzed almost completely in 1 N hydrochloric acid. In the accompanying diagram are plotted the curves characterizing the degree of hydrolysis of the salts of fuchsone, 2-hydroxyfuchsone, 4'-hydroxyfuchsone (benzaurin) and 4',4"-dihydroxyfuchsone (aurin) in solutions of hydrochloric acid with strengths ranging from 1 N to 10 N.

This diagram clearly demonstrates that in respect of stability of the salts to hydrolysis, 2-hydroxyfuchsone is very much closer to fuchsone than to benzaurin or aurin.

2-Hydroxyfuchsone also resembles unsubstituted fuchsone more closely in respect of ease of transformation into the corresponding carbinol derivative. As already pointed out [10], fuchsones and their carbinols are in a state of labile equilibrium. The ease of hydration of fuchsones depends, however, on the number of hydroxyl groups in

para-positions of the benzene rings of the fuchsone complex. Aurin and benzaurin undergo complete conversion to the carbinols when in an alkaline medium. With sufficiently high alkali concentration, the initially formed colored alkaline salts are completely converted into the colorless salts of the carbinols. Solutions of aurin are completely decolorized at a pH exceeding 12; solutions of benzaurin at a pH exceeding 10. But fuchsones not containing hydroxyl groups are hydrated even in a neutral medium, even if dissolved in an organic solvent to which water is added. It was found that the susceptibility of 2-hydroxyfuchsone to hydration in neutral solutions is as great as, if not greater than, that of fuchsone. Consequently the hydrolysis of acid-onium salts of aurin and benzaurin yields free dyes. Hydrolysis of similar salts of fuchsone yields a mixture of fuchsone itself and 4-hydroxytriphenylcarbinol [11]. Hydrolysis of the acid-onium salt of 2-hydroxyfuchsone results, however, in nearly complete formation of the carbinol derivative, 2,4-dihydroxytriphenylcarbinol (V).

Thanks to this behavior we were able to effect the preparation of 2,4-dihydroxytriphenylcarbinol (V) far more easily and with a very much greater yield than achieved by Bayer [6]. On triturating 2-hydroxyfuchsone hydrochloride with water, or better with sodium acetate solution, a colorless flocculent precipitate of 2,4-dihydroxytriphenylcarbinol is formed. The latter is converted by heating into 2-hydroxyfuchsone, so that the crystallization of 2,4-dihydroxytriphenylcarbinol must be performed very carefully with avoidance of excessive heating. The best procedure for crystallization is to dissolve the substance in benzene containing a trace of water and to heat to 60°. On slow cooling the carbinol separates in the form of colorless crystals. During the melting point determination the crystals gradually turn yellow, but in a rapid melting point determination they melt sharply at 124-125°.

The stability of 2,4-dihydroxytriphenylcarbinol is low. When heated it dehydrates to form 2-hydroxyfuchsone. When treated with hydrochloric acid it forms the hydrochloride of 2-hydroxyfuchsone. 2,4-Dihydroxyfuchsone is soluble in alkali, but the solution gradually turns cloudy, more rapidly on heating, due to formation of benzophenone. The latter collects in oily drops which solidify on standing.

2-Hydroxyfuchsone is likewise very unstable. It hydrates very easily, and when heated it decomposes with formation of benzophenone; we were consequently unable to isolate 2-hydroxyfuchsone in the analytically pure form. When heated in glacial acetic acid, 2,4-dihydroxytriphenylcarbinol forms an orange solution of 2-hydroxyfuchsone, but addition of water to the same solution leads to the reverse process of hydration with formation of a mixture of fuchsone and the carbinol. Heating of the 2,4-dihydroxytriphenylcarbinol with acetic acid followed by vacuum distillation of the solvent results in partial decomposition of the fuchsone. Partial decomposition also takes place when 2,4-dihydroxytriphenylcarbinol is dehydrated in the absence of a solvent in vacuum without heating; in our investigation we therefore isolated 2-hydroxyfuchsone in the form of its more stable hydrochloride or bisulfite compound.

From 2,4-dihydroxytriphenylcarbinol we also prepared its diacetyl derivative (VIII). This is more stable, and after crystallization from benzene it is obtained as colorless crystals melting sharply at 178-180°. The same acetyl derivative is obtained from 2-hydroxyfuchsone hydrochloride by heating with acetic anhydride and anhydrous sodium acetate, or from free 2-hydroxyfuchsone by heating with acetic anhydride. In the latter case, however, the purification of the acetyl derivative calls for several recrystallizations, because, for the reasons indicated above, 2-hydroxyfuchsone itself is contaminated with products of its own decomposition.

Investigation of 2-hydroxyfuchsone and its derivatives, and a comparison of them with aurin and benzaurin, show that the properties of hydroxyfuchsone derivatives essentially depend not only on the presence of hydroxyl groups and their number but also on their position.

The presence of hydroxyl groups in the p-positions of the benzene rings of the fuchsone grouping results in greater stability of the acid-onium salts of hydroxyfuchsone dyes. Apart from that, such hydroxyfuchsone dyes are more stable in the free state and undergo hydration only in a strongly alkaline medium with formation of colorless carbinol derivatives. 2-Hydroxyfuchsone, which contains the hydroxyl group in the quinoid ring in the o-position to the central carbon atom of the fuchsone complex, more closely resembles fuchsone (free from hydroxyl groups) in respect of stability of the acid-onium salt; moreover, 2-hydroxyfuchsone is very susceptible to hydration and therefore, unlike aurin or benzaurin, dissolves in dilute alkali to give the colored salt of hydroxyfuchsone and the colorless salt of the corresponding carbinol. In a neutral medium 2-hydroxyfuchsone also hydrates even more easily than the unsubstituted fuchsone.

From the foregoing considerations it follows that the hydroxyl group in the 2-position of the quinoid ring differs markedly from the hydroxyl group in the p-position of the benzene rings in its influence on the properties of hydroxyfuchsones. A possible reason for this is the development of a hydrogen bond with a blocking effect

between the hydroxyl group in the 2-position and the neutral carbon atom.

EXPERIMENTAL

Bisulfite compound of 2-hydroxyfuchsone. 11 g resorcinol is dissolved in 15 ml glacial acetic acid and to the solution is added, with cooling, 16.5 g freshly distilled benzophenone chloride. The vessel is closed with a stopper fitted with an elongated capillary and left to stand in a cold place for 2 days. The reaction proceeds with evolution of hydrochloric acid. The reaction mixture thickens and acquires a crimson color much darker than the color of solutions of benzaurin hydrochloride.

To the resultant reaction mixture is added 50 ml saturated solution of sodium bisulfite and 200 ml 15% sodium chloride solution. This mixture is heated to the boil and after addition of 1-2 g animal charcoal it is filtered. Cooling results in separation of a crystalline precipitate of the colorless bisulfite compound of 2-hydroxyfuchsone. The precipitate is filtered, washed with a little cold water and purified by recrystallization from water. Yield 25 g.

The bisulfite compound of 2-hydroxyfuchsone crystallizes from water in colorless crystals containing 1.5 moles water of crystallization. After dehydration it melts at 193-195° with decomposition. It is readily soluble in water and almost insoluble in organic solvents. The aqueous solutions turn yellow when heated, and when diluted with water a milky-white turbidity is formed due to hydrolysis of the bisulfite compound and hydration of the resultant fuchsone to the corresponding carbinol. Reaction with hydrochloric acid gives 2-hydroxyfuchsone hydrochloride.

The water of crystallization and the sodium content were determined on the substance dried to constant weight in the desiccator.

0.4879 g substance: 0.0308 g H_2O. 0.7955 g substance: 0.1390 g Na_2SO_4. 6.9196 g substance: 0.1582 g Na_2SO_4. Found %: H_2O 6.31; Na 5.66, 5.57. $C_{19}H_{17}O_3NaHSO_3 \cdot 1\frac{1}{2} H_2O$. Calculated %: H_2O 6.66; Na 5.68.

2-Hydroxyfuchsone hydrochloride. 25 g bisulfite derivative is dissolved in 150 ml water and impurities are filtered off. The filtrate is cooled and addition is made, with intensive stirring and external cooling, of 150 ml strong hydrochloric acid. The dark-red flocculent precipitate is filtered, well pressed, and washed with 15% hydrochloric acid solution. The precipitate is dried under vacuum and stored in a vacuum desiccator over calcium chloride. Yield 20 g.

Properties: Deep-scarlet crystalline powder, m.p. in a normal determination 105-107°. On slow heating gas is evolved and the color deepens at 80-85°. In water it rapidly hydrolyzes with simultaneous hydration. It dissolves with a crimson color in glacial acetic acid, amyl acetate, and ether. When traces of water are present in the solvents, decolorization takes place due to hydrolysis and hydration. When heated in hydrochloric acid it decomposes with formation of benzophenone.

Resistance to hydrolysis: 0.01 g substance is dissolved in 10 ml alcohol. To 0.1 ml portions of the solution are added lots of 10 ml hydrochloric acid with normalities of 11, 5, 3, 2 and 1.

Similar experiments were carried out for comparison with aurin, benzaurin, and fuchsone. After standing for one hour for attainment of equilibrium, colorimetric determinations were made of the color intensities which characterized the content of nonhydrolyzed hydrochloride. A solution in 10 N acid was used as standard. The results are presented in the table.

2,4-Dihydroxytriphenylcarbinol. 18 g bisulfite compound of 2-hydroxyfuchsone is dissolved in 150 ml hot water. After cooling, addition is made to the solution, with intensive stirring, of 150 ml concentrated hydrochloric acid. The precipitate of hydrochloride is filtered, washed with 15% hydrochloric acid and then transferred to a porcelain mortar in which is introduced 15 g sodium acetate and a little water. A resinous brown mass is formed which on trituration gradually whitens and subsequently changes into a viscous homogeneous suspension. This is transferred to a beaker, 150 ml water is added and the whole left for 24 hours in the cold. The bright precipitate of carbinol is filtered and washed with water. Without being dried, the product is put into benzene and warmed to 70°; the benzene layer is poured off from the aqueous layer through an ordinary filter. Cooling of the benzene solution brings out colorless crystals of 2,4-dihydroxytriphenylcarbinol; these are filtered and dried in a vacuum desiccator. Yield 8.7 g (67% of the theoretical).

Properties: Colorless or slightly yellow crystals with m.p. 123-124° (on rapid determination). Slow heating

to 75-80° results in marked darkening and softening due to the transformation into 2-hydroxyfuchsone. It is soluble in alcohol, ether, chloroform and hot benzene, almost insoluble in water, gasoline and petroleum ether. When treated with strong hydrochloric acid it is converted into the salt of 2-hydroxyfuchsone. Heating with glacial acetic acid gives an orange solution of 2-hydroxyfuchsone. The latter is also obtained by heating the carbinol above 80°. On heating with alkali it decomposes with formation of benzophenone.

Color Intensity of Hydrochlorides of some Hydroxyfuchsone Dyes

Dye	Normality of HCl				
	10	5	3	2	1
Aurin	100	100	–	–	90
Benzaurin	100	95	–	80	50
2-Hydroxyfuchsone	100	90	40	15	0
Fuchsone	100	80	15	5	0

0.0872 g substance: 0.2509 g CO_2; 0.0437 g H_2O. 0.0831 g substance: 0.2592 g CO_2; 0.0452 g H_2O. 0.0970 g substance: 6.8 ml 0.1 N NaOH. 0.1228 g substance: 8.5 ml 0.1 N NaOH.* Found %: C 78.52, 78.55; H 5.61, 5.28; (OH) 11.92, 11.77. $C_{19}H_{16}O_3$. Calculated %: C 78.08; H 5.48; (OH) 11.65.

2,4-Diacetoxytriphenylcarbinol. 30 g 2,4-dihydroxytriphenylcarbinol is boiled with 30 ml acetic anhydride. After dissolving, the carbinol solution develops an orange color which gradually lightens. Heating for an hour results in a light-yellow solution which is poured into 200 ml water. With progressive decomposition of the acetic anhydride the acetyl derivative separates in the form of clots which are filtered, washed with water and crystallized from benzene. Yield almost quantitative.

The colorless crystals melt sharply at 178-180°. Soluble in benzene and glacial acetic acid; insoluble in water. Relatively stable when treated with hydrochloric acid. With hydrochloric acid the substance saponifies in solution in glacial acetic acid with formation of 2-hydroxyfuchsone hydrochloride. It is saponified by heating with alkali but this process is accompanied by decomposition of the resultant 2,4-dihydroxytriphenylcarbinol.

0.0861 g substance: 0.2319 g CO_2; 0.0422 g H_2O. 0.0758 g substance: 0.2045 g CO_2; 0.0366 g H_2O. Found %: C 73.50, 73.62; H 5.48, 5.40. $C_{23}H_{18}O_5$. Calculated %: C 73.40; H 5.32.

SUMMARY

2-Hydroxyfuchsone can be prepared by condensation of benzophenone chloride with resorcinol; this reaction gives 2-hydroxyfuchsone hydrochloride. For the purpose of isolation and purification it is more convenient to prepare the bisulfite compound, from which the pure hydrochloride can be obtained by treatment with strong hydrochloric acid.

2-Hydroxyfuchsone only forms acid salts. It rapidly hydrates when treated with alkali to form the salt of 2,4-dihydroxytriphenylcarbinol. This carbinol derivative is also formed by hydration of 2-hydroxyfuchsone also in a neutral medium, as well as on hydrolysis of the hydrochloride.

The hydrochloride is only stable in concentrated solutions of strong acids. On addition of water the salt hydrolyzes more easily than the salt of hydroxyfuchsone dyes containing hydroxyl groups in the para-positions of the benzene rings of the fuchsone grouping (benzaurin and aurin). In contrast to the latter, hydrolysis of the hydrochloride is accompanied by hydration.

Acetylation of 2-hydroxyfuchsone and 2,4-dihydroxytriphenylcarbinol results in formation of 2,4-diacetoxytriphenylcarbinol.

2-Hydroxyfuchsone is unstable in storage. It readily hydrolyzes, and when heated it splits up with formation of benzophenone. 2-Hydroxyfuchsone can be kept in the form of its hydrochloride or, better still, in the form of its bisulfite compound.

A compound of 2-hydroxyfuchsone with benzaurin or aurin shows that in 2-hydroxyfuchsone the hydroxyl group on the quinoid nucleus in the o-position to the central carbon atom of the fuchsone grouping appears to be blocked, possibly due to a hydrogen bond.

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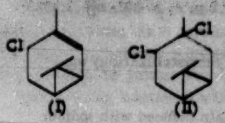
dΔ³-CARENE DICHLORIDE

B. A. Arbuzov and V. A. Frinovskaya

In a series of interesting papers recently published by D. V. Tishchenko and co-workers [1,2], a study was made of the action of chlorine on terpene hydrocarbons in presence of hydrogen chloride-binding substances. In the reaction of chlorine with dΔ³-carene in presence of sodium bicarbonate, D. V. Tishchenko and A. Khovanskaya [3] isolated from the reaction products an unsaturated monochloride and a dichloride; the latter could not be isolated in the pure form. The authors ascribe structure (I) to the monochloride. They do not give any data for the structure of the dichloride.



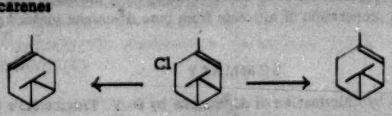
(I) (II)

Recently we have also studied the action of chlorine on terpene hydrocarbons in presence of hydrogen chloride-binding materials. In the chlorination of dΔ³-carene we isolated, apart from the monochloride, a dichloride in a purer form than was got by Tishchenko and Khovanskaya, and we determined its structure by reconversion to carene with the aid of finely divided sodium as a chlorine-binder. The so-prepared hydrocarbon gave a nitrosate with m.p. 143.5-144.0°, identical with the nitrosate of dΔ³-carene, and in the same yields as from pure dΔ³-carene. The preparation of dΔ³-carene from the dichloride indicates that the latter has the structure (II)

The unsaturated monochloride separated from the products of chlorination has constants fairly close to those reported by Tishchenko and Khovanskaya. Reduction of the monochloride with sodium in methyl alcohol at a temperature not exceeding 50° [4] gave a hydrocarbon which was not perfectly pure but whose constants were close to those of dΔ³-carene.

Fractions of the hydrocarbon gave good yields of the nitrosate of dΔ³-carene with m.p. 143.5-144.5°, indicating the presence of considerable amounts of Δ³-carene.

The formation of Δ³-carene by reduction of the monochloride is not inconsistent with the formula (I) proposed by Tishchenko and Khovanskaya since the reduction of allyl chlorides by metals in alcohol is accompanied by an allyl rearrangement [5], and in the case of reduction of monochloride (I) we should expect the formation of Δ⁹- and Δ⁶-carenes



which could not be separated by fractionation due to the closeness of the boiling points.

EXPERIMENTAL

dΔ³-Carene was separated from sulfate turpentine by fractionation in a column with 25 theoretical plates and had the constants: b.p. 63° (7 mm); d_4^{20} 0.8615; n_D^{20} 1.4729.

285 g Δ³-carene and 120 g sodium carbonate were mixed in a three-necked flask provided with a mechanical stirrer and immersed in freezing mixture (ice and salt). A slow stream of dry chlorine was passed through the Δ³-carene for 12 hours. After separation of the bicarbonate and the sodium chloride, the filtrate consisted of an aqueous layer (38.3 g) and an oil (315 g). Fractionation of the oil in vacuum using a Widmer dephlegmator yielded the following fractions (10 mm):

1) 49-59°, 75 g; 2) 59-80°, 52.5 g; 3) 80-84°, 26.7 g; 4) 84-85°, 28 g; 5) 85-120°, 70 g; 6) 120-153°, 29.2 g; residue 13 g.

Redistillation of the second to fourth fractions gave fractions with the following constants:

1) 72-74° (7 mm), 18 g; n_D^{20} 1.5028; d_4^{20} 0.9826; 2) 74-76° (7 mm), 37.2 g; n_D^{20} 1.5026; d_4^{20} 1.0047; MR_D 49.78. $C_{10}H_{16}Cl$ (three-membered ring); calculated 48.99.

0.1770 g substance: 0.1444 g AgCl. 0.1420 g substance: 0.01281 g active oxygen.* 0.1860 g substance: 0.01667 g active oxygen.* Found %: Cl 20.18; double bonds 0.96, 0.95. $C_{10}H_{16}Cl_2$. Calculated %: Cl 20.82.

Reduction of the monochloride with sodium. 15 g monochloride in 200 ml absolute methyl alcohol was reduced by addition of sodium (20 g), care being taken that the temperature of the liquid did not rise above 50°. After the whole of the sodium had been added, an extra 50 ml methyl alcohol was added, and the whole poured into water and extracted with ether; the residue after removal of the ether was distilled. After three distillations the following fractions (7 mm) were obtained:

1) 50-54°, 7.5 g; 2) 54-74°, 1 g; 3) 74-75°, 2.3 g.

The first fraction was distilled over sodium to give (7 mm):

a) 42-46°; n_D^{20} 1.4700; d_4^{20} 0.8634, 1.2 g; b) 46-50°; n_D^{20} 1.4712; d_4^{20} 0.8572, 3.2 g; c) 50-58°; n_D^{20} 1.4738; d_4^{20} 0.8692, 2.5 g.

From all three fractions the nitrosate of Δ^3-carene (m.p. 143.5-144.5° without recrystallization) was prepared.

The third fraction with b.p. 74-75° (7 mm) contained 3.9% chlorine. It was again reduced with sodium in methyl alcohol and had: b.p. 62-68° (6 mm); n_D^{20} 1.4760; d_4^{20} 0.9029.

Isolation of carene dichloride. Fractions 5-6 of the product of chlorination of Δ^3-carene gave after fractionation a fraction (36 g) with b.p. 107-110° (7 mm); n_D^{20} 1.5052; d_4^{20} 1.1146; MR_D 55.11. $C_{10}H_{16}Cl_2$ (three-membered ring); calculated 54.32.

0.1392 g substance: 0.1918 g AgCl. Found %: Cl 34.12. $C_{10}H_{16}Cl_2$. Calculated %: Cl 34.3. Titration with perphthalic acid showed the absence of double bonds.

Regeneration of Δ^3-carene from the dichloride. 15 g metallic sodium was pulverized to dust in hot toluene. To the cooled toluene was carefully added 20 g dichloride. Considerable heat was developed and the reaction continued for 2.5 hours; after decantation and distillation of the toluene in vacuum the residue was distilled. B.p. 44-50° (7 mm); 6.8 g. The following fractions were obtained by distillation (7 mm):

1) 40-45°, 1.2 g and 2) 45-48°, 4.3 g; n_D^{20} 1.4755; d_4^{20} 0.8639; MR_D 44.29; calculated 44.13.

The second fraction (2.5 g) yielded, by Simonsen's method, 0.4 g nitrosate with m.p. 143.5-144.0 without recrystallization. Parallel preparation of nitrosate from pure Δ^3-carene yielded (from 2.5 g) 0.5 g nitrosate.

SUMMARY

1. The dichloride prepared by chlorination of dΔ^3-carene by D. V. Tishchenko's method is 3,4-dichlorocarane, since cleavage of chlorine with sodium gives Δ^3-carene.

2. Reduction with sodium in alcohol of the unsaturated monochloride obtained from dΔ^3-carene gives a mixture of Δ^3-carene and, apparently, Δ^4-carene, and the process is accompanied by an allyl rearrangement.

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NITRATION OF (1,2,3,4)-TETRAHYDRO-2-NAPHTHOIC ACID

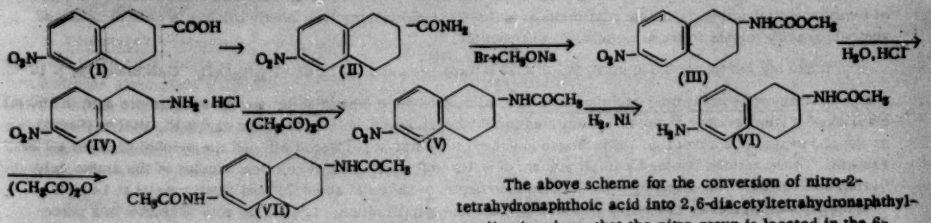
S. I. Sergievskaya and N. P. Volynsky

The presence of a substituent in the 2-position of the hydrogenated portion of the tetrahydronaphthalene molecule so changes the chemical properties of its nonhydrogenated ring that the usual reactions of aromatic compounds, such as nitration, proceed with extraordinary difficulty or entirely fail to give the anticipated results. It suffices to mention the repeated and unsuccessful efforts to nitrate the well-known ac-β-tetrahydronaphthylamine, or the difficulty in nitrating β-tetralone. In this investigation we have applied the nitration reaction to ac-2-tetrahydronaphthoic acid; using nitric acid of s.g. 1.5 no clear results were obtained, but by nitration with acid of s.g. 1.4-1.42 we succeeded in isolating a crystalline substance of acidic nature with m. pt. 196.5-197°. The yield, however, did not exceed 10%, the greater part of the ac-β-tetrahydronaphthoic acid being converted into a difficultly separable mixture of oily substances which we did not examine more closely.

The elementary analysis of the crystalline compound with m.pt. 196.5-197° showed it to correspond to a mononitrotetrahydronaphthoic acid, and its transformations (formation of an acid chloride, amide, ethyl ester, and – by catalytic reduction – aminotetrahydronaphthoic acid) confirmed the presence of both a carboxyl and a nitro group.

A preliminary determination of the position of the nitro group was made by decarboxylation of the aminotetrahydronaphthoic acid obtained from the nitro acid by the route indicated above. Decarboxylation was performed by dry distillation of the amino acid with barium hydrate at atmospheric pressure; the sole reaction product was β-naphthylamine since decarboxylation was accompanied by dehydrogenation of the tetrahydronaphthalene ring. These results established that the amino group (and consequently the nitro group) is in the 6- or 7- position of tetrahydronaphthalene.

The position of the nitro group was definitely established by the following transformations: The amide of nitrotetrahydro-2-naphthoic acid (II) was converted into the corresponding urethane (III) by the action of bromine and sodium methylate; without purification, (III) was subjected to saponification with the help of concentrated hydrochloric acid. These reactions yielded the hydrochloride of nitro-ac-2-tetrahydronaphthylamine (IV), not previously described in the literature; this nitroamine was converted into its acetyl derivative (V), and the nitro group in the latter was reduced to the amino group (VI). Acetylation of the resultant compound yielded the known, 2,6-diacetyltetrahydronaphthylenediamine (VII) [1]:



The above scheme for the conversion of nitro-2-tetrahydronaphthoic acid into 2,6-diacetyltetrahydronaphthylenediamine shows that the nitro group is located in the 6-position of the tetrahydronaphthalene ring and the nitro acid which we have prepared is 6-nitro-(1,2,3,4)-tetrahydro-2-naphthoic acid (I).

EXPERIMENTAL

6-Nitro-ac-tetrahydro-2-naphthoic acid. 70 g ac-tetrahydro-2-naphthoic acid with m. pt. 90-92° is added in one portion to 350 ml HNO_3, s.g. 1.42 and the mixture is heated (to initiate the reaction) to 38-40°, after which this tem-

perature is maintained for two hours. At the conclusion of the reaction the solution is cooled to −5° and the resultant precipitate is filtered off. Yield 13.5 g with m. pt. 175-180°. The filtrate is heavily diluted with water which precipitates a yellow resin; the latter is separated from the aqueous acid solution and triturated with toluene. The insoluble precipitate is filtered off, giving a further 5 g of substance with m. pt. 175-185°. Nitration by the above-described method (in two lots) of 185 g ac-tetrahydro-2-naphthoic acid with m. pt. 90-92° gave 30 g of substance with m. pt. 170-180°, which separated from the reaction mixture and 20 g substance with m. pt. 150-170° which separated on diluting the acid solution with water.

The 20 g substance with m. pt. 150-170° was recrystallized from toluene to give 15 g nitro acid with m. pt. 188-191° (I). The toluene mother liquor yielded (after distilling off the toluene) 3 g of substance with m. pt. 160-215°.

The 30 g of substance with m. pt. 170-180° was also recrystallized from toluene. Yield 24 g with m. pt. 178-188° (II).

The 24 g of (II) was dissolved in 10% sodium carbonate solution and fractionally precipitated with hydrochloric acid, giving 15 g with m. pt. 178-190° (first fraction) and 9 g with melting point 175-215° (second fraction). The first fraction was recrystallized from alcohol to give a yellowish substance with m. pt. 190-193°. The substance with m. pt. 190-193° was combined with substance (I) with m. pt. 188-191° and twice recrystallized from alcohol. There was obtained 22 g 6-nitro-ac-tetrahydro-2-naphthoic acid with m. pt. 196.5-197°. It was in the form of light-yellow crystals readily soluble in ether, acetone and (with heating) alcohol, less easily soluble in hot toluene, very sparingly soluble in alcohol and toluene in the cold

6.675 mg substance: 0.386 ml N_2 (21.5°, 721.0 mm). 4.069 mg substance: 8.965 mg CO_2; 1.851 mg H_2O. Found %: N 6.36; C 60.09; H 5.09. $C_{11}H_{11}O_4N$. Calculated %: N 6.34; C 59.74; H 4.97.

Ethyl ester of 6-nitro-ac-tetrahydro-2-naphthoic acid. 1 g of 6-nitro-ac-tetrahydro-2-naphthoic acid is heated with 15 ml absolute ethyl alcohol and 3 drops concentrated H_2SO_4 at the boiling point for 6 hours. A bulky crystalline precipitate comes down on cooling and is filtered at the pump and washed with a small amount of absolute alcohol. Yield 1 g substance with m. pt. 83°. After recrystallization from absolute alcohol the ethyl ester of 6-nitro-ac-tetrahydro-2-naphthoic acid forms silky, colorless needles with m. pt. 83.5-84°. Readily soluble in acetone, ether, benzene, hot ethyl alcohol; very sparingly soluble in cold ethyl alcohol.

5.410 mg substance: 0.284 ml N_2 (22.0°, 721.0 mm). Found %: N 5.75. $C_{13}H_{15}O_4N$. Calculated %: N 5.62.

6-Nitro-ac-tetrahydro-2-naphthoyl chloride. 1 g 6-nitro-ac-tetrahydro-2-naphthoic acid is heated with 4 ml $SOCl_2$ at 85-90° for 3 hours, after which the excess of thionyl chloride is removed in vacuum and the residue recrystallized from CCl_4. The acid chloride forms colorless needles with m. pt. 113-113.5°, readily soluble in benzene, acetone and CCl_4 (hot), very sparingly soluble in petroleum ether and cold CCl_4.

6-Nitro-ac-tetrahydro-2-naphthoic acid amide. 7 g 6 nitro-ac-tetrahydro-2-naphthoyl chloride is dissolved in absolute benzene and the solution is shaken with strong aqueous ammonia solution. The precipitate of amide is filtered and washed with water. Yield 5.5 g with m. pt. 206-207°. After two crystallizations from alcohol the amide of 6-nitro-ac-tetrahydro-2-naphthoic acid melts at 209-210°. Colorless crystals, poorly soluble in cold alcohol and acetone, readily soluble in the same solvents when heated.

6.520 mg substance: 0.745 ml N_2 (21.0°, 726.5 mm). Found %: N 12.68 $C_{11}H_{12}O_3N_2$. Calculated %: N 12.73.

6-Amino-ac-tetrahydro-2-naphthoic acid. A solution of 4.4 g 6-nitro-ac-tetrahydro-2-naphthoic acid in 150 ml ethyl alcohol (temperature about 40°) is agitated in a hydrogen atmosphere in presence of 5 g Ni catalyst (Raney). At the end of the reduction (1350 ml hydrogen absorbed) the catalyst is filtered off, and the alcohol distilled off in vacuum. To the residue is added a small amount of water which precipitates colorless needles of the amino acid. During the melting point determination the substance begins to soften at about 70° and finally melts at 140-145°. This behavior is apparently due to the presence of water of crystallization. The amino acid is heated in a porcelain beaker at 130-140° until no more water vapor comes off. The cooled solid melt is pulverized and recrystallized from toluene to give 3.3 g 6-amino-ac-tetrahydro-2-naphthoic acid with m. pt. 144-145°. The compound is readily soluble in methyl and ethyl alcohols and acetone, and, on heating, in water and toluene.

6.407 mg substance: 3.37 ml 0.01 N H_2SO_4. Found %: N 7.36. $C_{11}H_{13}O_2N$. Calculated %: N 7.33.

Decarboxylation of 6-amino-ac-tetrahydro-2-naphthoic acid. 1.5 g of the amino acid is triturated with 4 g

$Ba(OH)_2$ and a very small quantity of methyl alcohol. The carefully dried mixture is dry-distilled at the ordinary pressure. The distillate (a solid) is extracted with ether, the ethereal solution is washed with alkali solution and dried with potassium hydroxide. The residue after distillation of the ether is a yellow substance with m. pt. 90-95°. After recrystallization from petroleum ether it melts at 107-109° (light-orange leaflets). This melting point is close to that of 2-naphthylamine. A mixed sample with 2-naphthylamine melts at 109-111° (pure 2-naphthylamine has m. pt. 110-112°).

6-Acetamino-ac-tetrahydro-2-naphthoic acid. A small amount of 6-amino-ac-tetrahydro-2-naphthoic acid is acetylated with acetic anhydride under gentle heating (50°) for 30 minutes. The reaction mixture is extracted with boiling water. Needlets of the acetyl derivative come down after cooling. 6-Acetamino-ac-tetrahydro-2-naphthoic acid recrystallizes from water as colorless needles with m. pt. 206-207°, readily soluble in alcohol and in hot water.

5.665 mg substance: 0.318 ml N_2 (21.0°, 726.5 mm). Found %: N 6.23. $C_{13}H_{15}O_3N$. Calculated %: N 6.01.

6-Nitro-ac-tetrahydro-2-naphthylamine (hydrochloride). 5.5 g 6-nitro-ac-tetrahydro-2-naphthoic acid amide is dissolved with heating in 50 ml dry methyl alcohol. The hot solution of the amide is poured into a sodium methylate solution prepared from 1.15 g Na and 25 ml dry methyl alcohol. To the mixture is gradually added 4.0 g Br_2. The reaction temperature is held at 40-50° for 10 minutes, and then acetic acid is added until neutral to litmus. The alcohol is removed by heating on the water bath and the residue treated with water to remove mineral salts. There is obtained 5.8 g substance with m. pt. 135-175°, consisting of a mixture of urethane and unreacted amide.

2.8 g of the product with m. pt. 135-175° is saponified by heating with 12 ml strong hydrochloric acid at 130-140° for 4 hours in a sealed tube. The contents of the tube (crystalline precipitate) are filtered off and the precipitate treated with boiling water. The hot solution is quickly filtered. The water-insoluble substance is 6-nitro-ac-tetrahydro-2-naphthoic acid with m. pt. 195-198° (0.8 g). To the aqueous filtrate is added a large amount of concentrated hydrochloric acid. After a short time light-yellow needlets of 6-nitro-ac-tetrahydro-2-naphthylamine hydrochloride come down (1.1 g). Evaporation of the hydrochloric acid mother liquor yields a further 0.3 g. The hydrochloride crystallizes nicely from ordinary alcohol (it is insoluble in absolute alcohol). It chars when heated in a capillary to 230° (does not melt).

7.000 mg substance: 0.752 ml N_2 (20.0°, 721.0 mm). Found %: N 11.87. $C_{10}H_{12}O_2N_2 \cdot HCl$. Calculated %: N 12.24.

Acetyl-(6-nitro-ac-tetrahydro-2-naphthylamine). A mixture of 0.9 g 6-nitro-ac-tetrahydro-2-naphthylamine hydrochloride, 5 ml benzene, 1.5 ml acetic anhydride and 1 g dry potassium acetate is heated for 30 minutes. On cooling, the precipitate is filtered off and washed with benzene and water. Recrystallization from aqueous alcohol gives 0.4 g of substance with m. pt. 173-175°. From the benzene solution separates an additional 0.3 g with m. pt. 170-171° (after recrystallization from aqueous alcohol). Both lots are combined and recrystallized from ethyl acetate, giving 0.35 g acetyl-(6-nitro-ac-tetrahydro-2-naphthylamine) with m. pt. 176-177°, in the form of fine leaflets with a light-yellow color, readily soluble in acetone, alcohol, and, on heating, water and ethyl acetate. The mother liquor yields a further 0.2 g with m. pt. 170-171°.

3.967 mg substance: 3.30 ml 0.01 N H_2SO_4. Found %: N 11.65. $C_{12}H_{14}O_3N_2$. Calculated %: N 11.96.

Diacetyl-(2,6-tetrahydronaphthylenediamine). 0.35 g acetyl-(6-nitro-ac-tetrahydro-2-naphthylamine) is dissolved in 20 ml absolute ethyl alcohol. To the solution is added 4 g Raney Ni catalyst and the mixture shaken in a hydrogen atmosphere until absorption of the required amount of hydrogen (100 ml). At the end of the reduction the catalyst is filtered off and the alcohol distilled off in vacuum. The residue is triturated with 0.6 ml acetic anhydride and 2 ml absolute benzene. A white crystalline precipitate is formed with m. pt. 239°; recrystallized from aqueous alcohol, the m. pt. is 240.5-241°, corresponding to the m.p of diacetyl-(2,6-tetrahydronaphthylenediamine).*

4.708 mg substance: 3.80 ml 0.01 N H_2SO_4. Found %: N 11.30. $C_{16}H_{18}O_2N_2$. Calculated %: N 11.38.

SUMMARY

Nitration of ac-β-tetrahydronaphthoic acid gives 6-nitro-(1,2,3,4)tetrahydro-2-naphthoic acid; its structure was established and preparations were effected of its simplest derivatives and of the corresponding 6-amino-(1,2,3,4)-tetrahydro-2-naphthoic acid.

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[1]. Windaus, Ber., 57, 1731 (1924).

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* Windaus gives 240° for the m.p. of diacetyl-(2,6-tetrahydronaphthylenediamine) [1].

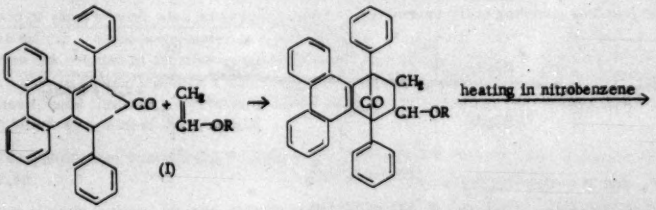
DIENE SYNTHESIS WITH ANISYLCYCLONE AND SOME OTHER CYCLONES

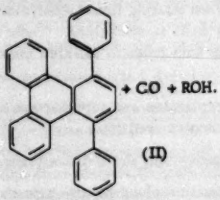
V. S. Abramov and L. A. Shapshinskaya

Phenylated derivatives of cyclopentadienone – cyclones – are extremely reactive substances. They possess a cis-butadienoid system of conjugated double bonds activated by the carbonyl group. Such a system is bound to readily undergo the diene synthesis. This has actually proved to be the case by a series of investigators who reacted cyclones with various dienophiles: maleic anhydride [1], p-quinone, α-naphthoquinone [2], allyl alcohol, allyl chloride [3], phenylated derivatives of ethylene [1] and acetylene, phenylpropiolic aldehyde, phenylpropiolic acid, the methyl ester of acetylenedicarboxylic acid, acetylene [4], etc.

The diene synthesis with cyclones proceeds at moderate temperatures and with relatively brief heating. Particular ease of addition is noted in the case of phencyclone, the reactions with which sometimes proceed at room temperature.

Reactions of cyclones with compounds containing the vinyl radical have previously been investigated by V. S. Abramov [5] who described reactions of vinyl ethers and esters, as well as of vinyl bromide, with acecyclone, cyclone, piperylcyclone, and aceanthrenecyclone. The reactions with vinyl ethers proceed at 180-200°. In the reactions of vinyl ethers with all of the above-listed cyclones the endocarbonyl bridge is ruptured and cleavage occurs of either a molecule of alcohol (in the case of vinyl ethers) or of a molecule of acid (in the case of esters) to yield the corresponding hydrocarbons. A similar course is followed with unsaturated compounds of the type of vinyl bromide. Phencyclone (I) adds on both vinyl ethers and esters with considerably greater ease than other cyclones. Unlike other cyclones, phencyclone reacts with vinyl ethers and vinyl bromide to give addition products in which the endocarbonyl bridge is retained in accordance with the scheme [8]:





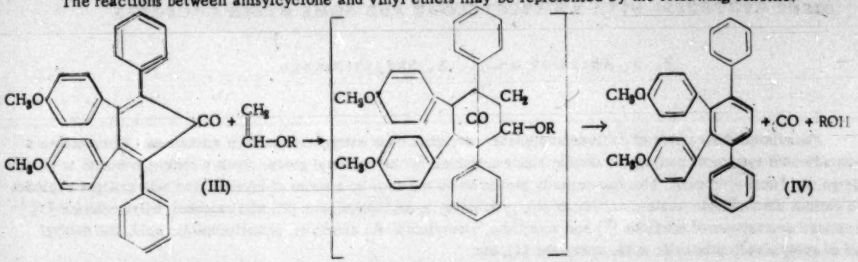
When the products of addition of vinyl compounds to phencyclone are heated in high-boiling solvents such as tetrahydronaphthalene and nitrobenzene, the endocarbonyl bridge is broken and cleavage occurs of a molecule of alcohol or acid to give a hydrocarbon (II).

The purpose of the present investigation was the study of the behavior of anisylcyclone (III) in diene syntheses with vinyl compounds of the type of $CH_2{=}CHX$ where X is any noncarbon atom.

Diene syntheses of anisylcyclone with vinyl ethers and esters were performed in sealed tubes in a medium of benzene. The reaction mass in the tubes was heated to a temperature of 150-160° for 10 to 20 hours.

The investigation has revealed that the diene synthesis of anisylcyclone with vinyl compounds proceeds analogously to that of tetracyclone and other cyclones (except phencyclone), i.e., in the conditions of the diene synthesis the endocarbonyl bridge is broken and cleavage occurs of an alcohol (with ethers), an acid (with esters), or hydrogen bromide (in the case of vinyl bromide).

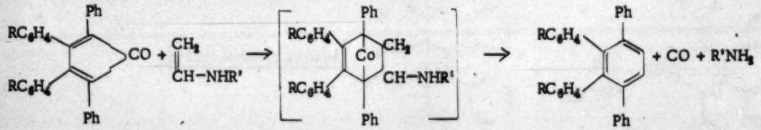
The reactions between anisylcyclone and vinyl ethers may be represented by the following scheme:



Reactions were performed with vinyl n-butyl ether, vinyl isoamyl ether, trivinyl glyceryl ether, vinyl phenyl ether, vinyl acetate and vinyl bromide. All these reactions give one and the same product: 1,4-diphenyl-2,3-di-(p-methoxyphenyl)-benzene (IV). The identity of the 1,4-diphenyl-2,3-di-(p-methoxyphenyl) benzene obtained in the various diene syntheses was established by mixed melting point determinations, when no depression was observed. The hydrocarbon forms white, well-defined, lustrous crystals with m. pt. 180-181°.

In addition we studied the action of vinylamino compounds containing a tertiary nitrogen atom on cyclone and anisylcyclone as representatives of dienes. Vinylamino derivatives (N-vinylethanolamine and N-vinylcaprolactam) were selected because an amino group has an effect on electron displacement contrary to that of other vinyl compounds (vinyl ethers). We therefore hoped to obtain products of addition to cyclones. Contrary to our expectations the N-vinyl derivatives react with cyclones in accordance with the usual scheme, i.e., with cleavage of the endocarbonyl bridge and detachment of the corresponding amine or of caprolactam. This behavior of vinylamino derivatives may probably be explained by the influence of the other groups in their molecules. Owing to lack of experimental material we are unable to draw a definite conclusion.

The reaction proceeds according to the scheme:



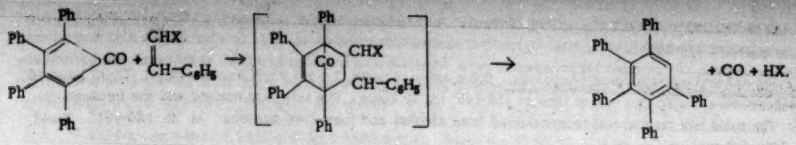
where R = H or OCH_3, and R' = $-CH_2-CH_2OH$ or $CH_2-CH_2-CH_2$ / $CO-CH_2-CH_2$

The reactions were performed in sealed tubes in a benzene medium and at temperatures of 170-200°. The hydrocarbon, 1,2,3,4-tetraphenylbenzene is easily isolated in the pure state when starting from tetracyclone; the same applies to 1,4-diphenyl-2,3-di-(p-methoxyphenyl) benzene when starting from anisylcyclone. These hydrocarbons were identified with the help of the mixed melting point determinations with products isolated from other similar diene syntheses.

It was not possible to isolate in the pure state the detached ethanolamine and caprolactam because small amounts were used in the experiments and they resinified in the experimental conditions.

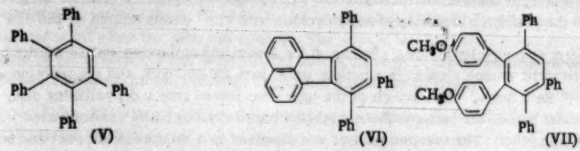
We also investigated the diene synthesis of cyclones with ω-bromostyrene and ω-nitrostyrene.

It was to be expected that the reactions would proceed by the usual mechanism with rupture of the endocarbonyl bridge and cleavage of hydrogen bromide (in the case of ω-bromostyrene) and of nitrous acid (in the case of ω-nitrostyrene):



where X = Br or NO_2.

The reaction of tetracyclone and ω-nitrostyrene has been described in the literature [8]; we have repeated it and extended it to acecyclone and anisylcyclone. The reactions of ω-bromostyrene with cyclone, acecyclone and anisylcyclone were also studied. The reactions were conducted under roughly the same conditions as described above. In all cases hydrocarbons were isolated which we identified through the mixed melting point determinations. The following were obtained: Pentaphenylbenzene (V) in reactions with cyclone; 1,4,5-triphenyl-2,3-(1,8-naphthylene) benzene (VI) in reactions with acecyclone; and 1,4,5-triphenyl-2,3-di-(p-methoxyphenyl) benzene (VII) in reactions with anisylcyclone.



(V) (VI) (VII)

The presence of hydrogen bromide and oxides of nitrogen was detected qualitatively when the tubes were opened.

The experiments entitle us to regard the described reactions as general reactions for cylcones taking place according to the usual scheme of the diene synthesis with vinyl compounds.

We extend our sincere thanks to Corresponding Member of the Academy of Sciences of the U.S.S.R., B. A. Arbuzov for his interest in our work and his general guidance.

EXPERIMENTAL

Action of vinyl n-butyl ether on anisylcyclone [7]. 0.5 g anisylcylcone, 2 ml vinyl n-butyl ether (b. pt. 93.8°) and 15 ml dry benzene were heated in a sealed tube at 150-160° for 14 hours. The reaction was considered at an end when the contents of the tube were decolorized. The tube was then opened, the benzene distilled off, and alcohol added to the residue when a light-pink, finely crystalline precipitate came down. This was filtered off and washed several times on the filter with ether. After recrystallization from acetone the product melted at 180-181°. Yield 0.4g or 80% of theory.

0.1284 g substance: 0.4070 g CO_2; 0.0684 g H_2O. Found %: C 86.45; H 5.96. $C_{32}H_{26}O_2$. Calculated %: C 86.88; H 5.88.

Action of vinyl isoamyl ether on anisylcyclone. 0.5 g anisylcyclone, 2 ml vinyl isoamyl ether (b. pt. 105-110°) and 15 ml dry benzene were heated in a sealed tube at 150-160° for 23 hours until the contents had decolorized. The tube was opened, the benzene distilled off. On standing, the residue deposited fine, pink crystals. Recrystallization from acetone gave stout, lustrous, colorless crystals which melted at 180-181°. Yield 0.37 g or 73% of theory. A mixed sample with the above-described product melted at 180-181°.

The substance prepared was 1,4-diphenyl-2,3-di-(p-methoxyphenyl) benzene.

Action of vinyl phenyl ether on anisylcyclone. 0.5 g anisylcyclone, 2 ml vinyl phenyl ether (b. pt. 153-154°) and 15 ml dry benzene were heated in a sealed tube at 147° for 70 hours until the contents decolorized. The tube was opened and the benzene distilled off from the reaction products. From the residue was obtained a crystalline product which after recrystallization from acetone melted at 180-181°. Yield 0.33 g or 65% of theory. A mixture with the above-described preparations of 1,4-diphenyl-2,3-di-(p-methoxyphenyl) benzene melted at 180-181°.

Action of trivinyl glyceryl ether on anisylcyclone. 0.5 g anisylcyclone, 2 ml trivinyl glyceryl ether and 15 ml dry benzene were heated in a sealed tube at 110-120° for 20 hours and at 140-150° for 20 hours until the red color of anisylcyclone had disappeared. The tube was opened and the benzene distilled off. To the residue was added alcohol and immediately a fine, pale-pink powder came down. It was filtered and recrystallized from

acetone. M. pt. 180-181°. Yield 0.3 g or 60% of theory. In admixture with 1,4-diphenyl-2,3-di-(p-methoxyphenyl) benzene it melted at 180-181°.

Action of vinyl acetate on anisylcyclone. 0.5 g anisylcyclone, 1.5 ml vinyl acetate (b. pt. 72-73°) and 15 ml dry benzene were heated in a sealed tube at 155-165° for 30 hours. The tube was opened and the benzene distilled off. The solidified residue was recrystallized from alcohol and then from acetone. M. pt. 180-181°. Yield 0.38 g or 76% of theory.

A mixed specimen with other products of similar reactions (1,4-diphenyl-2,3-di-(p-methoxyphenyl)-benzene melted at 180-181°.

Action of vinyl bromide on anisylcyclone. 0.5 g anisylcyclone, 1 ml vinyl bromide and 15 ml dry benzene were heated in a sealed tube at 120° for 10 hours and at 150° for 10 hours. The contents of the tube partly resinified. When the tube was opened it was noticed that pressure had developed and gaseous hydrogen bromide came off. The benzene was distilled off. The residue was diluted with ether and a dark precipitate came down which was filtered off and recrystallized from acetone. The product did not contain halogen when tested by burning on copper oxide. After three recrystallizations from acetone the melting point was constant at 180-181°. Yield 0.25 g or 50% of theory. A mixed sample with the products of reaction of anisylcyclone with vinyl ethers melted at 180-181°.

Action of N-vinylethanolamine on cyclone. 0.4 g cyclone, 0.3 g N-vinylethanolamine and 15 ml dry benzene were heated in a sealed tube under carbon dioxide in a boiling water bath for 10 hours, and the reaction was then completed by heating at 168° for 8 hours. The contents of the tube were poured into a crystallizing dish, and following removal of the greater part of the benzene there separated brown crystals badly contaminated with resin. The resin was washed out with ether. The reaction product was dissolved in a mixture of alcohol and benzene and digested with animal charcoal. Cooling of the filtrate was followed by separation of well-formed, lustrous-white crystals, with m. pt. 189-190°. Yield of pure product 0.15 g or 37.4% of theory. The Lassaigne test for nitrogen gave a negative result. A mixed sample with 1,2,3,4-tetraphenylbenzene melted at 190-191°.

Action of N-vinylcaprolactam on cyclone. 0.4 g cyclone, 0.2 g N-vinylcaprolactam and 15 ml dry benzene were heated in a sealed tube under carbon dioxide at 160-180° for 8 hours and the reaction then completed by heating at 200° for 8 hours. The reaction products were transferred to a crystallizing dish and the benzene evaporated at room temperature, leaving a crystalline mass saturated with resin. The latter was washed out with ether. The crystalline residue was recrystallized from a mixture of alcohol and benzene. M. pt. 189-190°. Yield 0.2 g or 50% of theory. A mixed sample with 1,2,3,4-tetraphenylbenzene melted at 190°.

Action of N-vinylethanolamine on anisylcyclone. 0.4 g anisylcyclone, 0.3 g N-vinylethanolamine and 15 ml dry benzene were heated in a sealed tube under carbon dioxide at 170° for 10 hours. The contents were poured into a crystallizing dish and the benzene evaporated. The residue of dark-brown resin dissolved readily in ether. At the bottom of the dish remained a fine, dark powder. Careful washing with ether and recrystallization from alcohol-acetone and then from acetone gave crystals with m. pt. 180-181°. The Lassaigne test for nitrogen gave a negative result. Yield of pure product 0.1 g or 25% of theory. A mixed sample with the product of reaction of anisylcyclone with vinyl ethers melted at 180-181°.

Action of N-vinylcaprolactam on anisylcyclone. 0.4 g anisylcyclone, 0.2 g N-vinylcaprolactam and 15 ml dry benzene were heated in a sealed tube at 160° for 10 hours and then at 180° for 10 hours. A crystalline residue contaminated with resin was obtained after removing the benzene. The resin was washed out with ether. The crystalline residue was recrystallized from acetone-alcohol and then from acetone. Lustrous crystals with m. pt. 180-181°. Nitrogen was absent. Yield of pure product 0.3 g or 75% of theory. A mixed specimen with the above-described product melted at 180-181°.

Action of ω-nitrostyrene on cyclone [7]. 0.5 g cyclone, 0.3 g ω-nitrostyrene and 10 ml dry benzene were heated in a sealed tube at 170° for 30 hours until the color had disappeared. The solvent was distilled off and to the residual light-yellow oil was added ether to bring down white crystals which after recrystallization from alcohol melted at 244-245°. Yield 0.3 g or 50.8% of theory. The product did not contain nitrogen. No depression in melting point when mixed with pentaphenylbenzene.

Action of ω-nitrostyrene on acecyclone. 1 g acecyclone, 0.6 g ω-nitrostyrene and 15 ml dry benzene were heated in a sealed tube at 170° for 30 hours. The benzene was distilled off. The residual resin was diluted with ether when the resinous portion dissolved to leave a residue of yellow powder. The latter was filtered, well-washed with ether and recrystallized from a mixture of equal parts of alcohol and benzene and then from petrol M. pt. 194-195°. Yield 0.77 g or 68.7 % of theory. No depression of melting point in admixture with the product of reaction of bromostyrene and acecyclone.

Action of ω-nitrostyrene on anisylcyclone. 0.5 g anisylcyclone, 0.3 g ω-nitrostyrene and 15 ml dry benzene were heated in a sealed tube at 160° for 10 hours and then at 180° for 10 hours. Pressure was released when the tube was opened and the odor of oxides of nitrogen was noticed. After removal of the benzene the residual crystalline product was well-washed with ether and recrystallized from a mixture of alcohol and acetone to give stout white crystals with m. pt. 222-223°. Nitrogen was absent. Yield of pure product 0.4 g or 70% of theory.

0.0914 g substance: 0.2926 g CO_2; 0.0486 g H_2O. Found %: C 87.31; H 5.91. $C_{29}H_{24}O_2$. Calculated %: C 88.03; H 5.79

Action of ω-bromostyrene on cyclone. 0.5 g cyclone, 1 ml ω-bromostyrene and 15 ml dry benzene were heated in a sealed tube at 150-160° for 12 hours and at 180-190° for 15 hours until the color had disappeared. On opening the tube a large amount of hydrogen bromide came off. The benzene was distilled off to a third of its volume and alcohol was added to the residue The product crystallized and was filtered off and recrystallized twice from a mixture of equal parts of methyl alcohol and benzene. M. pt. 244-245°. Yield 0.45 g or 83.3% of theory. The melting point was not depressed in admixture with pentaphenylbenzene.

Action of ω-bromostyrene on acecyclone. 1 g acecyclone, 1.5 ml ω-bromostyrene and 15 ml dry benzene were heated in a sealed tube at 150-160° for 12 hours and at 180-190° for 15 hours. A large amount of hydrogen bromide came off when the tube was opened. The solvent was distilled off and ether added to the residue; crystals came down at once These were filtered and twice recrystallized from a mixture of equal parts of methyl alcohol and benzene M. pt. 194-195°. Yield 0.8 g or 66.6% of theory.

0.1016 g substance: 0.3520 g CO_2; 0.0504 g H_2O. Found %: C 94.47; H 5.56. $C_{34}H_{28}$. Calculated %: C 94.88; H 5.22.

Action of ω-bromostyrene on anisylcyclone. 0.3 g anisylcyclone, 0.4 g ω-bromostyrene and 15 ml dry benzene were heated in a sealed tube under carbon dioxide at 150-160° for 15 hours and at 180-190° for 10 hours. A small amount of hydrogen bromide came off when the tube was opened. The solvent was distilled off and ether added to the resinous residue. The resin dissolved and crystals remained at the bottom of the crystallizing dish. These were twice recrystallized from alcohol-acetone. M. pt. 222-223°. Yield of pure product 0.2 g or 66.66% of theory. Halogen was found to be absent in the copper oxide test.

A sample mixed with the product of reaction of anisylcyclone with ω-nitrostyrene melted at 222-223° and did not show any depression.

SUMMARY

1. Anisylcyclone reacts with vinyl ethers and esters and with vinyl bromide according to the diene synthesis reaction.

2. During the diene synthesis the endocarbonyl bridge is ruptured and cleavage occurs of alcohol (in the case of vinyl ethers) and of acid (in the case of vinyl esters), or of hydrogen bromide (in the case of vinyl bromide); all these reactions yield one and the same product – 1,4-diphenyl-2,3-di-(p-methoxyphenyl)benzene (VIII).

3. Tetracyclone and anisylcyclone react with N-vinyl derivatives (N-vinylethanolamine and N-vinylcaprolactam) according to the usual synthesis with vinyl compounds with rupture of the endocarbonyl bridge and cleavage of amine or caprolactam.

4. Tetracyclone, acecyclone and anisylcyclone react with ω-bromostyrene and ω-nitrostyrene according to the usual scheme with rupture of the endocarbonyl bridge and cleavage of hydrogen bromide or the elements of nitrous acid.

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INVESTIGATION OF THE ALKALOIDS OF MAKROTOMIA ECHIOIDES

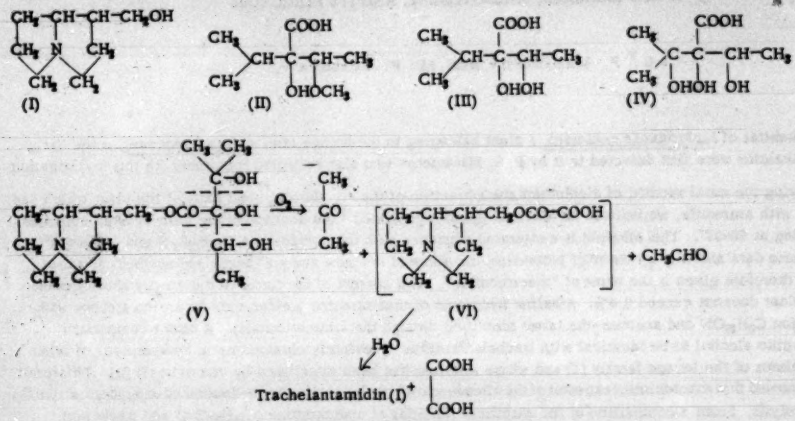
I. A NEW ALKALOID, MACROTOMINE, AND ITS STRUCTURE

G. P. Menshikov and M. F. Petrova

The habitat of Makrotomia echioides, a plant belonging to the borage family (Borraginaceae), is the Transcaucasus. Alkaloids were first detected in it by P. S. Massagetov who also collected specimens for this investigation.

Applying the usual method of dichloroethane extraction of the dry above-ground parts of the plant which had been treated with ammonia, we isolated an alkaloid which crystallized from acetone in the form of large colorless prisms, melting at 96-97°. This alkaloid is a saturated substance with the composition $C_{18}H_{31}O_5N$ and $[\alpha]_D$ −6.9°. Judging by these data and also by its other properties, the alkaloid is a new and previously undescribed substance, and we have therefore given it the name of "macrotomine". The content of the latter in the air-dry above-ground parts of the plant does not exceed 0.4%. Alkaline hydrolysis of macrotomine yielded only an amino alcohol with the composition $C_9H_{19}ON$ and acetone (the latter identified through the semicarbazone). A direct comparison showed the amino alcohol to be identical with trachelantamidine, previously obtained by us by hydrolysis of other alkaloids of plants of the borage family [1] and whose structure had been established by one of us (I) [2]. This result of hydrolysis showed that macrotomin is an ester of the already known trachelantamidine and an unknown acid which breaks down on hydrolysis. From a comparison of the empirical formulas of macrotomine ($C_{18}H_{31}O_5N$) and trachelant amidine ($C_9H_{19}ON$), it is easily seen that the unknown acid must have the composition $C_7H_{14}O_5$. Three acids are already known, however, out of those obtained by hydrolysis of plant alkaloids from the borage family—heliotrinic [3], trachelantic [4] and viridifloric [5], the basic skeleton of which also contains 7 carbon atoms. The structural formula (II) was established by one of us for heliotrinic acid, and structural formula (III) for viridifloric acid. These formulas show that heliotrinic acid only differs from trachelantic acid in containing a methoxyl in place of a hydroxyl group, while viridofloric acid has precisely the same structure as trachelantic acid of which it is a diastereomer. On the basis of this similarity in structure it is extremely probable that the unknown acid of macrotomine has a similar structure and only differs from trachelantic acid in containing another hydroxyl group which is located at the carbon atom linked to the two methyl groups, as evidenced by the formation of acetone on hydrolysis. In short, we can assume that the acid of macrotomine has the structure of 2-methyl-2,3,4-trihydroxypentane-3-carboxylic acid (IV). For confirmation of our assumption we selected the method of oxidation of the alkaloid with iodic acid. If the acid really has structure (IV), then macromotine itself must have structure (V), and oxidation with iodic acid should therefore proceed with consumption of two atoms of oxygen and formation of acetone, the acid oxalate of trachelantamidine (VI) and acetaldehyde [see structure (V); the broken line shows the place of rupture]. Finally, all this could only occur if trachelantamidine itself did not enter into reaction with iodic acid. In order to test this last point, we performed an experiment in which the oxidation of trachelantamidine with iodic acid was attempted. It was found that the iodic acid was not reduced at all. Furthermore, a similar experiment was performed with macrotomine itself, and it was found that the amount of iodic acid required for oxidation (as determined by titration) was almost precisely two moles per mole of macrotomine, corresponding to one mole of oxygen per mole of alkaloid. These data, which confirmed our above assumption about the structure of macrotomine, prompted us to institute experiments on the oxidation of relatively large amounts of macrotomin for the purpose of a detailed investigation of the resultant products. At first we carried out the oxidation of macrotomine in a strongly acid medium in presence of free sulfuric acid. By this means we isolated and identified the acetone and acetaldehyde anticipated on the basis of formula (V). Concerning the anticipated acid oxalate of trachelantamidine, we isolated in its place the products of its saponification, i.e., trachelantamidine and oxalic acid. It can easily be seen that these results do not conflict with the above postulates and that they form equally convincing evidence of the correctness of our claim that macrotomine has the structure (V). Apart from that, they show that the acid oxalate of trachelantamidine is apparently an extremely unstable substance readily susceptible to

saponification. Assuming that the saponification of this ester proceeded because of the presence of free sulfuric acid in the solution, we carried out experiments on the oxidation of macrotomine with sodium iodate, but even by this method it was impossible to isolate the oxalate of trachelantamidin in the pure form. However, immediately after the oxidation the solution contained a considerable amount of free oxalic acid which could be isolated in the form of the calcium salt. But in addition the solution contained, apparently, the ester as evidenced by the formation of a fresh fairly large quantity of free oxalic acid after saponification of a solution from which all of the free oxalic acid had previously been precipitated in the form of the calcium salt. All this points to the great instability of the acid oxalate of trachelantamidin which, of course, greatly complicates its separation in the pure form.



EXPERIMENTAL

Isolation and purification of macrotomine. 5 kg pulverized, air-dry, above-ground parts of the plant were processed with 10% ammonia solution until there was a strong odor of ammonia and then exhaustively extracted with dichloroethane (test with silicotungstic acid solution). From the dichloroethane solution the base was extracted with 10% sulfuric acid solution. The acid extract was treated with 20% ammonia solution until strongly alkaline and extracted with chloroform. The chloroform extract was dried with sodium sulfate and filtered before the chloroform was distilled off completely on the water bath. The residual viscous oil crystallized at once when triturated with acetone. The crystalline precipitate was filtered at the pump, washed with a little acetone and recrystallized three times from five times the amount of acetone. After this purification the substance was in the form of large, colorless prisms melting at 95-97° after drying in vacuum (50-55°, 15 mm). The total yield was about 20 g.

0.758 g substance: 10 ml alcohol; 1 1 dm; α_D −0.52°, $[\alpha]_D$ −6.9°. 3.830 mg substance; 8.421 mg CO_2; 3.037 mg H_2O. 3.616 mg substance: 7.987 mg CO_2; 2.933 mg H_2O. 7.693 mg substance: 0.325 ml N_2 (25°, 736 mm). 8.768 mg substance: 0.369 ml N_2 (27°, 730 mm). 6.666 ml substance: 1.44 mg CH_4 (17°, 748 mm). Found %: C 59.96, 60.09; H 8.87, 9.07; N 4.67, 4.60; OH 15.2. $C_{15}H_{27}O_5N$. Calc.%: C 59.76; H 9.03; N 4.64; 3OH 16.94.

Macrotomine is very easily soluble in water and alcohol, less easily soluble in cold acetone and benzene, poorly soluble in ether.

Macrotomine picrate was prepared by mixing alcoholic solutions of the base and picric acid. After crystallization from alcohol the picrate had the form of light-yellow fine needles, melting without decomposition at 130-132°.

5.115 mg substance: 0.465 ml N_2 (22°, 756 mm). Found %: N 10.46. $C_{15}H_{27}O_5N \cdot C_6H_3O_7N_3$. Calculated %: N 10.56.

Saponification of macrotomine. 5 g of the alkaloid was dissolved in 20 ml of 2 N sodium hydroxide,

and the solution heated for 2 hours under a reflux condenser on the boiling water bath. The condenser was then placed in the sloping position and 10 ml was distilled off from the solution at normal pressure. To the distillate were added dry semicarbazide hydrochloride and sodium acetate. A crystalline precipitate at once appeared and was recrystallized from alcohol. It melted at 190° and did not depress the melting point of acetone semicarbazide. The alkaline solution from which the acetone had been distilled off with water was extracted with chloroform. The chloroform extract was dried with sodium sulfate and the chloroform distilled off to leave an oil which was distilled in vacuum (16 mm) at 142°. The distilled base was identified as trachelantamidin both from its properties and from the properties of the salts prepared from it.

The alkaline solution from which the trachelantamidin had been extracted with chloroform was treated with 20 ml 2 N hydrochloric acid solution, and the water was completely distilled off therefrom in vacuum (15 mm). The residue was finally dried by addition of absolute alcohol which was then distilled off, and the dried residue was extracted with hot absolute alcohol. The alcohol solution was filtered from inorganic salts and the solvent distilled off. There remained a viscous oil with an acidic character. All attempts to crystallize it or to prepare crystalline salts from it met with failure. Experiments were also carried out on the saponification of macrotomine with barium hydroxide in which the barium was removed in the form of carbonate, but negative results were likewise obtained. No substances, apart from acetone and trachelantamidin could be isolated in the pure state.

Oxidation of macrotomine with iodic acid in an acid medium. To 3 g of the alkaloid were added 40 ml 1 N sulfuric acid solution, 30 ml water and 5 g potassium iodate. The mixture was agitated on a shaking machine until the precipitate had completely dissolved, and the solution was left overnight at room temperature. The next morning the solution was divided into two parts, equal. One of these was placed in a Wurtz flask connected to a wash bottle containing dimedon solution which had been saturated at room temperature. The Wurtz flask was closed with a stopper through which passed a glass tube reaching to the bottom. A stream of air was slowly sucked through for four hours. The crystalline precipitate which separated from the dimedon solution was filtered off. After recrystallization from water it melted at 139-140° and did not depress the melting point of acetaldehyde aldimedon. The solution remaining after distillation of the acetaldehyde in an air stream was repeatedly extracted with ether. After removal of the solvent there remained a crystalline deposit which after recrystallization from water and sublimation was identified as oxalic acid. The solution from which the oxalic acid had been extracted with ether was treated with a large excess of 20% ammonia solution and exhaustively extracted with chloroform. The chloroform extract was dried with sodium sulfate and the chloroform distilled off, leaving an uncrystallizable oil which was identified by direct comparison as trachelantamidin.

The second part of the solution was treated with barium hydroxide until alkaline to phenolphthalein. The solution was freed from the precipitate by decantation and from it was distilled off, at the ordinary pressure, about 15 ml water. The distillate was treated with freshly prepared ammoniacal silver solution for removal of the acetaldehyde. A silver mirror was at once formed. After standing for three hours the precipitate was removed by decantation and from the solution was distilled (using a dephlegmator) 5 ml water at the ordinary pressure. To the distillate was added dry semicarbazide hydrochloride and dry sodium acetate. The resultant precipitate melted at 190° (from alcohol) and did not depress the m.p. of acetone semicarbazone.

Oxidation of macrotomine with sodium iodate. 1.2 g of the alkaloid was dissolved in 30 ml water; to the solution was added 1.9 g sodium iodate, and the whole left for 24 hours at room temperature. To the solution, which had a strong odor of acetaldehyde, was added strong calcium chloride solution. The precipitate was filtered, carefully washed with water, treated with 10 ml of 10% sulfuric acid solution and extracted several times with ether. The ether was driven off from the extract to leave a small amount of crystals identified as oxalic acid.

To the solution from which the free oxalic acid had been precipitated with calcium chloride was added 10 ml 20% sulfuric acid before heating for two hours on the boiling water bath. The hot solution was filtered from inorganic salts, cooled, and repeatedly extracted with ether. After removing the ether, there remained a fairly large amount of crystals, also identified as oxalic acid.

SUMMARY

1. A new crystalline alkaloid, macrotomine, $C_{18}H_{27}O_5N$, was isolated from the Transcaucasian plant Makrotomia echioides, belonging to the borage family. It melts at 95-97° and has m.p. 95-97° and $[\alpha]_D - 6.9°$.

2. Alkaline hydrolysis of macrotomine enables only an amino alcohol of the composition $C_8H_{15}ON$ and acetone to be isolated.

3. The isolated amino alcohol was found to be identical with trachelantamidine, preobtained by hydrolysis of the alkaloids trachelantamine and viridiflorine and for which the structure (I) had already been established.

4. The results of hydrolysis show that macrotomine is an ester of trachelantamidine and an unknown acid which decomposes on hydrolysis to form acetone.

5. Oxidation of macrotomine with iodic acid consumes one mole oxygen per mole alkaloid and yields acetone, trachelantamidine, oxalic acid and acetaldehyde, which points to structure (V) as the only possible one for macrotomine.

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DELSEMIDINE

IV. INVESTIGATION OF DELPHINIUM ALKALOIDS

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In the investigation of the amorphous mixtures remaining after separation of the crystalline portion of the total alkaloids from Delphinium semibarbatum [1], it was noted that an additional amount of the amino alcohol, delsine, can be obtained by their saponification in alkalies. In the acidic portion of the hydrolysis products, however, was found not delseminic acid (which would have pointed to the presence in the mixture of residues of the alkaloid, delsemine) but methylsuccinylanthranilic acid. A similar observation was made in work with the unseparated portion of the total alkaloids from D. creophilum* [2]. These facts support the belief that the above-mentioned plants possibly contain, in addition to delsemine and delsine, a third base with a structure close to that of delsemine. After some efforts, this alkaloid was actually isolated in the form of the crystalline salt of perchloric acid. The base itself, obtained by decomposition of the perchlorate, was amorphous. Apart from the perchlorate, the crystalline hydroiodide was isolated.

Elementary analysis of the base corresponds to $C_{27}H_{35}O_{10}N_2$. This formula is also confirmed by the summation of the formulas of hydrolytic decomposition of the alkaloid-delsine, $C_{20}H_{31}O_7N$ and methylsuccinylanthranilic acid, $C_{12}H_{13}O_5N$.

On comparing the properties of our alkaloid with the properties of the alkaloids isolated from other varieties of Delphinium, we noted that it closely resembles methyllycaconitine and delartine. The first was found by Goodson [4] in 1943 in Delphinium elatum, the second by Rabinovich and Konovalova [5] in Delphinium sp. (a varietal name not yet established). In the table are compared the physico-chemical constants of the above compounds.

Constants	Delsemidine	Delartine	Methyllycaconitine
Formula of base	$C_{27}H_{35}N_2O_{10}$	$C_{29}H_{33}N_2O_{11}$	$C_{37}H_{48}N_2O_{19}$
Melting point	122-130°*	110-130°	119-128°*
Specific rotation in alcohol	+46.6	+45.1	+49.1
Hydroiodide, dry, melting point	199-202	–	201
" " [α] in 1 N KOH	+18.7	–	+18.5
" " $[\alpha]_D$ 0.2 N KOH	+21.8	–	+24.4
" " $[\alpha]_D$ 0.024 N KOH	–	–	+31.2
" " $[\alpha]_D$ in alcohol	+22.6	–	–
Perchlorate, dry, melting point	194-195	188-190°	–
" " $[\alpha]_D$ in alcohol	+25.4	+25.08	–

According to this table the properties of all three alkaloids are so close that there would hardly appear to be any doubt that they are identical. But when comparing such compounds we must not omit an examination of the products of their saponification. All three bases are esters. Methyllycaconitine hydrolyzes when heated with alkali and forms methylsuccinylanthranilic acid and an amino alcohol which Goodson, from the similarity of some of its

* All the melting points have been corrected for the exposed part of the mercury.

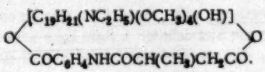
* In 1940 the botanist K. S. Afanasev [3] described a new variety of delphinium — Delphinium rotundifolium — from the northern slopes of the Turkestan mountains. It resembles D. oreophilum but differs from it mainly in its round quinquepartite lower leaves and in the character of its trimming. According to an examination by E. E. Korotkova, director of the botanical group of our institute, the material investigated by us more nearly resembles D. rotundifolium Afan. than D. oreophilum Huth.

properties, took to be lycoctonine. Although the cleavage with formation of methylsuccinylanthranilic acid is also consistent with our own data, there is little probability, as already shown [6], that the amino alcohols lycoctonine and delsin are identical.

On the other hand, although there is hardly any doubt of the identity between delartine and delsine [6], their esterifying acids — delartic and methylsuccinylanthranilic acids — exhibit a series of differing properties. When delartic acid is hydrolyzed in an acid medium it splits up into anthranilic acid and a crystalline substance with m.p. 170-172° whose structure has not yet been elucidated but which apparently contains three carbon atoms. But the acid which we isolated hydrolyzes under analogous conditions to anthranilic and methylsuccinic (m.p. 112°) acids.

On the basis of the above considerations, we propose to call our alkaloid "delsemidine". Whether or not it is identical with methyllycaconitine and delartine will only be decided after a direct comparison of specimens of all three alkaloids.

On the assumption that hydrolysis of delsemidine involves consumption of two equivalents of alkali and that the resultant acid is dibasic, the partially established formula of the alkaloid may be:



EXPERIMENTAL

Isolation of delsemidine. The amorphous mixture remaining after fractionation of the total alkaloids of Delphinium semibarbatum and separation of delsemine is extracted in the cold with small portions of ether. The combined ether extract of the alkaloids is separated into seven fractions by successive extraction with 1 N hydrochloric acid. To each fraction is added a saturated aqueous solution of ammonium perchlorate; from each fraction is at once precipitated a white, soft mass. The acid solutions containing the precipitates are placed in an ice chest. After two days the material in the first three fractions had solidified completely, and fine crystals had appeared on the walls. The crude delsemidine perchlorate was recrystallized from 5 parts of water and 15 parts methanol. The recrystallized salt was pulverized and covered with 10 parts water. Addition was then made of a few milliliters of concentrated ammonia solution. An excess of ammonia was avoided as far as possible. The separated friable precipitate was filtered at the pump, washed a few times with water, and dried in a vacuum desiccator over calcium chloride.

Separation of delsemidine from the total alkaloids of D.oreophilum is effected in a similar manner.

Delsemidine. Free delsemidine, dehydrated by drying in a vacuum at 105°, is a light, amorphous powder with a faint yellow color. It could not be recrystallized from any solvent. The alkaloid is very unstable to alkalies and acids. Even in low-boiling solvents its solutions rapidly darken when heated.

Delsemidine melts in the range 122-130° with frothing. The base is very easily soluble in alcohol, acetone, chloroform and benzene, fairly easily soluble in ether, sparingly soluble in petroleum ether and water.

0.4080 g substance: in 10 ml alcohol; l 10.0; α_D + 1.90°, $[\alpha]_D^{23}$ + 46.6°.

0.1262 g substance: 0.2994 g CO_2; 0.0850 g H_2O. 0.1200 g substance: 0.2850 g CO_2; 0.0808 g H_2O. 0.1042 g substance: 4.10 ml N_2 (23°, 727 mm). 0.1036 g substance: 4.15 ml N_2 (22°, 728 mm). Found %: C 64.74, 64.81; H 7.54, 7.53; N 4.36, 4.44. $C_{37}H_{50}O_{10}N_2$. Calculated %: C 65.08; H 7.38; N 4.10.

Delsemidine hydroiodide. 2.0 g delsemidine is dissolved in 4.0 ml alcohol and the solution acidified with a few drops of 10% hydriodic acid until weakly acid to Congo red. On the following day the contents of the flask are inthe form of a crystalline mass. The salt is drained at the pump and recrystallized from 70% alcohol. Delsemidine hydroiodide crystallizes in the form of very fine needlets containing 3 moles of water of crystallization and usually aggregating to yellow clusters.

0.9284 g substance: 0.0580 g H_2O (105°, in vacuum). Found %: H_2O 6.25. $C_{37}H_{50}O_{10}N_2 \cdot HI \cdot 3H_2O$. Calculated %: H_2O 6.25.

The dehydrated salt melts gradually at 199-202° (with decomposition). It is sparingly soluble in water and alcohol.

Goodson [4] determined the specific rotation of methyllycaconitine hydroiodide in potassium hydroxide solution and reported that $[\alpha]_D$ changes with the concentration of the alkali solution. This behavior was also observed with delsemidine but to a less marked degree.

0.2028 g substance: in 10 ml 0.9675 N alcoholic solution of KOH; l 10.0; α_D + 0.38°, $[\alpha]_D^{20}$ + 18.7°. 0.2017 g substance in 10 ml 0.1935 N alcoholic solution of KOH; l 10.0; α_D + 0.44°, $[\alpha]_D^{20}$ + 21.8°. 0.1994 g substance in 25 ml alcohol; l 10.0; α_D + 0.18°, $[\alpha]_D^{20}$ + 22.6°. 0.1264 g substance: 3.11 ml 0.05 N $AgNO_3$ (potentiometrically). 0.1324 g substance: 3.28 ml 0.05 N $AgNO_3$. Found %: I 15.61, 15.72. $C_{37}H_{56}O_{10}N_2 \cdot HI$ Calculated %: I 15.66.

Delsemidine perchlorate.* After repeated recrystallization from aqueous methanol, the perchlorate is in the form of fine platelets aggregated to large clusters. The salt crystallizes with 1.5 moles water. The dried salt melts at 194-195° with decomposition. Like the hydroiodide, the perchlorate is sparingly soluble in water and alcohol. The solutions have a slight violet fluorescence.

Saponification of delsemidine. Into a solution of 4.0 g delsemidine in 30 ml methanol is poured 11.8 ml of 1.0 N potassium hydroxide (2 equivalents), and the alcohol rapidly distilled off. When the main bulk of the alcohol was evaporated, 10 ml water is added to the residue. After a short time crystallization commences. The crystals are drained, washed with a few milliliters of water and recrystallized from 70% alcohol. The pure crystals have m.p. 139° and do not depress the melting point of delsin. The slightly yellow alkaline mother liquor is exhaustively extracted with ether for removal of traces of delsin, and is then acidified in the cold with 6 ml 1.0 N hydrochloric acid. On the following day the small brown precipitate is filtered off and addition is made to the solution of a further 6 ml of 1.0 N acid. The oil which then separates is left overnight and crystallizes. The filtered and dried crystals melt at 163-164°. A mixed sample with α-methylsuccinylanthranilic acid melts at 164-165°.

The crystals with m.p. 163-164° were recrystallized from hot water. The recrystallized acid melts at 170°. It does not depress the melting point of β-methylsuccinylanthranilic acid. When hydrolyzed in an acid medium, methylsuccinylanthranilic acid splits up into anthranilic and methylsuccinic acids.

SUMMARY

1. An alkaloid, $C_{37}H_{56}O_{10}N_2$, called "delsimidine" has been found in Delphinium semibarbatum and D. oreophilum (D. rotundifolium).

2. When hydrolyzed in alkalies, delsemidine splits up into the amino alcohol, delsin, and the dibasic methylsuccinylanthranilic acid.

3. The possible identity between the alkaloids delsemidine, delartine and methyllycaconitine is discussed.

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* 0.6806 g substance: 0.2520 g H_2O (105°, in vacuum). Found %: H_2O 3.70. $C_{37}H_{56}O_{10}N_2 \cdot HClO_4 \cdot 1.5H_2O$. Calculated %: H_2O 3.34. 0.2364 g substance in 25 ml solution 60% alcohol; l 10.0; α_D + 0.24°, $[\alpha]_D^{25}$ + 25.4°. 0.1466 g substance: 0.0272 g AgCl. 0.1254 g substance: 0.0228 g AgCl. Found %: Cl 4.59, 4.50. $C_{37}H_{56}O_{10}N_2 \cdot HClO_4$. Calculated %: Cl 4.53.

** See Consultants Bureau translation, p. 189.

*** See Consultants Bureau translation, p. 1059.

**** See Consultants Bureau translation, p. 1389.

SYNTHESIS AND POLYMERIZATION OF UNSATURATED ORGANOSILICON COMPOUNDS

II. SYNTHESIS OF TRIALLYLETHYLSILANE

B. I. Yakovlev and N. V. Vinogradova

Triallylethylsilane, not previously described in the literature, was prepared by the action of ethyltrichlorosilane on allyl magnesium bromide in ether solution:

$$3CH_2{=}CH{-}CH_2MgBr + C_2H_5SiCl_3 \longrightarrow (CH_2{=}CH{-}CH_2)_3Si(C_2H_5) + 3MgClBr$$

The yield (on the ethylchlorosilane) reached 60%.

The method of preparation is similar to that described for diallyldiethylsilane [1].

A mixture of 48.4 g dry allyl bromide and 120 ml ether is gradually added to 8.1 g magnesium turnings in a round-bottomed flask fitted with a stirrer, mercury seal and reflux condenser. Slow addition is then made to the allyl magnesium bromide of 9.1 g ethyltrichlorosilane (b.p. 98.5-100.5°). The mixture is then heated for 5 hours, and after cooling it is decomposed with a 25% solution of NH_4Cl (in ice). The ether layer is collected, dried over calcium chloride, and distilled to remove the ether. The residue is distilled in vacuum through a column. Yield 5.9 g substance with b.p. 105-106° at 34 mm.

The silicon content was determined by the previously described procedure [1]: Combustion of 0.2-0.3 g substance with a mixture of conc. H_2SO_4 and HNO_3 and estimation in the form of SiO_2. The double bonds were determined by titration with bromine in carbon tetrachloride; concordant results were also obtained with Kaufmann's solution. A bromine number of 266.9 was found (calculated 265.9).

Triallylethylsilane has the following constants:

B.p. 105-106° at 34 mm; d_4^{20} 0.8237; n_D^{20} 1.4723. 0.107 g substance: 0.0352 g SiO_2, 0.1950 g substance: 0.5230 g CO_2; 0.1936 g H_2O. 0.3198 g substance: 15.36 g benzene: Δt 0.60°. Found %: Si 15.37; C 73.15; H 11.11; M 177.0. $C_{11}H_{20}Si$. Calculated %: Si 15.28. C 73.34; H 11.21; M 180.06.

SUMMARY

Triallylethylsilane has been prepared by reaction of allyl magnesium bromide with ethyltrichlorosilane, and its constants are detailed.

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INVESTIGATION OF THE ALKALOIDS OF TURNEFORCIA SIBIRICA

1. A NEW ALKALOID, TURNEFORCINE

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A liquid alkaloid has been isolated from the Transcaucasian plant, Turneforcia sibirica, a member of the borage family. The substance forms well-crystallized salts (picrate, hydrochloride and chloroplatinate). Isolation was effected by the usual method of dichloroethane extraction of the pulverized above-ground parts of the plant after treatment with ammonia solution. The isolated alkaloid, which is present in the plant to the extent of not more than 0.07%, has the composition $C_{15}H_{21}O_5N$; its hydrochloride melts at 169-170° and has $[\alpha]_D^{20}$ −58.59° (water). Since the alkaloid differs from all previously described bases, we propose the new name of "turneforcine".* Like all the alkaloids which we have isolated from plants of the borage family, it is an ester. Alkaline hydrolysis yielded angelic acid and a saturated amino alcohol of the composition $C_8H_{15}O_2N$ which, following the proposed nomenclature, we give the name of "turneforcidine". Hydrolytic splitting of turneforcine may therefore be represented by the following equation:

$$C_{15}H_{21}O_5N + H_2O = C_8H_{15}O_2N + C_5H_8O_2.$$

Up to now three saturated amino alcohols with the same composition have been known; they were obtained by hydrolysis or other chemical transformations of alkaloids of plants of the Borraginaceae and Compositae families, and have the names platynecine [2], dihydroxyheliotridane [3] and hastanecine [4]. A direct comparison established that turneforcidine was not identical with any of these. Consequently, turneforcine is an ester of angelic acid and the amino alcohol, turneforcidine.

EXPERIMENTAL

Isolation and purification of turneforcine. 6 kg air-dry, pulverized above-ground parts of the plant were moistened with 10% ammonia solution until there was a strong odor of ammonia, and then exhaustively extracted with dichloroethane. The alkaloid was extracted from the dichloroethane solution with sulfuric acid solution. Traces of dichloroethane were removed from the acid solution by extraction with ether, the ether solution was separated, and the acid solution treated with a large excess of 20% ammonia prior to fresh extraction with ether. The ether extract was dried with sodium sulfate and the ether distilled off to leave a residue of uncrystallizable oil. To this was added a cold saturated solution of picric acid in alcohol until acid to methyl orange. A crystalline picrate came down at once and was drained at the pump, washed with alcohol, and recrystallized once from alcohol, giving 7.9 g light-yellow lustrous platelets with m.p. 199.5-201°. The melting point did not change on further recrystallization.

7.415 mg substance: 0.782 ml N_2 (21°, 732 mm). 7.480 mg substance: 0.786 ml N_2 (21°, 732 mm). Found %: N 11.80, 11.76. $C_{15}H_{21}O_5N \cdot C_6H_3O_7N_3$. Calculated %: N 11.96.

The free base was prepared from the picrate by treatment with 10% hydrochloric acid followed by exhaustive extraction of the picric acid with ether. The colorless acid solution was treated with excess of 20% ammonia solution. The alkaloid was extracted with ether, the ether extract dried with sodium sulfate and the ether completely distilled off. From 7 g picrate was obtained 3.4 g of a colorless uncrystallizable oil.

Turneforcine hydrochloride. The alkaloid obtained via the picrate was dissolved in a small amount of absolute alcohol and to the solution was added an alcoholic solution of hydrochloric acid until acid to Congo. Dry ether was then added. On standing at 0° the solution deposited crystals which were reprecipitated with dry ether from absolute alcohol. After reprecipitation the hydrochloride formed colorless needles melting at 169-170°.

0.3619 g substance: 5 ml water; 1 0.5 dm; α_D −2.12°; $[\alpha]_D$ −58.59.

* Reference is made in the literature to two alkaloids with the composition $C_{15}H_{21}O_5N$, isolated from Senecio sylvaticus and Senecio Sarracenicus [1], but unfortunately they have been so superficially investigated and so briefly described that it is impossible to decide whether or not they are identical with turneforcine.

3.958 mg substance: 8.188 mg CO_2; 2.788 mg H_2O. 3.403 mg substance: 7.006 mg CO_2; 2.406 mg H_2O. 7.065 mg substance: 0.334 ml N_2 (24°, 740 mm). 0.2815 g substance: 10.12 ml 0.1 N solution $AgNO_3$. Found %: C 56.42, 56.14; H 7.88, 7.91; N 5.28; Cl 12.76, $C_{13}H_{21}O_3N \cdot HCl$. Calculated %: C 56.59; H 8.06; N 5.08; Cl 12.86.

Turneforcine chloroplatinate. To an alcoholic solution of the alkaloid acidified with hydrochloric acid was added 10% platinum chloride solution. On standing the solution deposited crystals which were recrystallized from 1% aqueous hydrochloric acid. Yellow leaflets, m. pt. 154.5-155.5°.

Saponification of turneforcine. 2 g of the alkaloid was treated with 20 ml of 10% sodium hydroxide solution and refluxed on a boiling water bath until dissolved (about 3 hours). The cooled solution was treated with 20% hydrochloric acid solution until acid to Congo and then extracted with ether. The ether extract was dried with sodium sulfate and the ether distilled off, using a dephlegmator. A light-yellow oil remained which at once crystallized when cooled. After recrystallization from water it melted at 43-44° and was identified as angelic acid by direct comparison. The acidic solution from which the angelic acid had been extracted was evaporated and dried in vacuum. The dry residue was extracted with absolute alcohol. The alcoholic solution was filtered and inspissated in vacuum to a volume of 5-6 ml. Addition to this concentrate of sufficient ether to cause turbidity resulted in deposition of crystals (1.2 g) which after reprecipitation from absolute alcohol with dry ether had the form of thin colorless needles with m. pt. 116°.

5.208 mg substance: 3.919 mg AgCl. 6.374 mg substance: 4.768 mg AgCl. Found %: Cl 18.62, 18.51. $C_8H_{15}O_2N \cdot HCl$. Calculated %: Cl 18.32.

The free base was obtained from this hydrochloride by dissolving in a little water, adding a slight excess of dry sodium carbonate to the solution, and completely distilling off the water in vacuum. The residue was dried by distilling off absolute alcohol from it in a vacuum. The dry residue was digested with dry acetone and the hot acetone solution was filtered. Crystals came down on cooling. These were recrystallized twice from 50 times the amount of acetone. The base formed snow-white needles with m. pt. 118.5-120°. A mixture with hastanecine (m. pt. 113-114°) melted at about 85-90°.

0.0528 g substance: 0.791 ml methyl alcohol; l 0.5 dm; α_D −0.35°; $[\alpha]_D$ −10.5°.

5.059 mg substance: 11.264 mg CO_2; 4.225 mg H_2O. 3.564 mg substance: 7.978 mg CO_2; 3.040 mg H_2O. 6.795 mg substance: 0.549 ml N_2 (20°, 730 mm). 6.570 mg substance: 0.534 ml N_2 (20°, 730 mm). Found %: C 60.72, 61.05; H 9.34, 9.54; N 9.04, 9.07. $C_8H_{15}O_2N$. Calculated %: C 61.09; H 9.61; N 8.92.

The base is saturated in character; it does not deoxidize potassium permanganate in 10% sulfuric acid solution.

SUMMARY

1. Isolation was effected from Turneforcia sibirica (Borraginaceae family) of a new, optically active alkaloid with the composition $C_{13}H_{21}O_3N$, named "turneforcine". It was characterized in the form of salts with the following constants: Hydrochloride − m. pt. 169-170°, $[\alpha]_D$ −58.59°; picrate − m. pt. 199.5-201°; chloroplatinate − m. pt. 154.5-155.5°.

2. Alkaline hydrolysis of turneforcine gave angelic acid and a new, hitherto undescribed, saturated amino alcohol with the composition $C_8H_{15}O_2N$, named "turneforcidine".

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*See Consultants Bureau translation, p. a-137.

INVESTIGATIONS ON ISOQUINOLINE COMPOUNDS

V. SYNTHESIS OF THE NATURAL ALKALOID, EMETINE*

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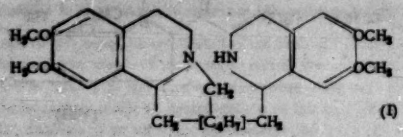
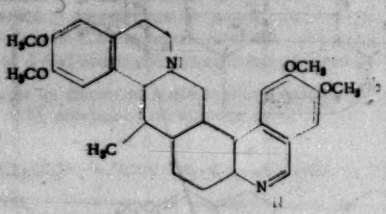
L. I. Zakharkin and N. A. Preobrazhensky

The alkaloid emetine, like morphine, strychnine and curarine, is one of those very important natural compounds whose structure had not hitherto been confirmed by synthesis. It was first prepared in 1817 [1] and in 1879 it was isolated by Podvysotsky [2] in the pure form. As a result of the studies of various transformations of the alkaloid performed by numerous authors over a period of over 100 years [3], it was established that the emetine molecule contains two tetrahydroisoquinoline nuclei linked by a group of seven carbon atoms [4] (I):

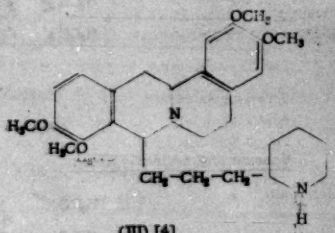


(I)

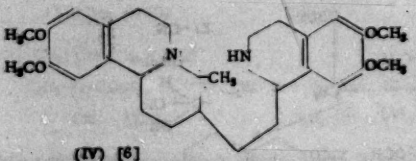
Further elucidation of the structure of emetine proved to be extremely difficult and the following structures were advanced by various authors and then rejected:



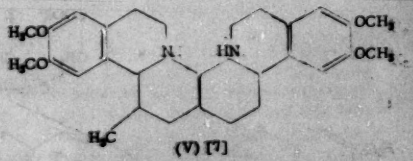
(II) [5]



(III) [4]



(IV) [6]



(V) [7]

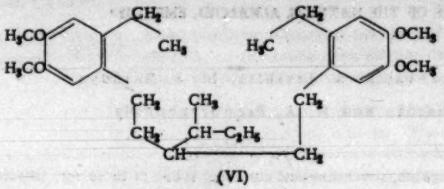
Although the above formulas are consistent with a series of chemical reactions of emetine, not one of them fully reflects the properties of the alkaloid.

In the years 1948-1950 a very large number of papers were published which aimed at clarifying the structure of the central portion of the emetine molecule [8]. In the course of these investigations a systematic study was made

* We described the synthesis of emetine for the first time in Proc. Acad. Sci. U.S S.R., 75, 539 (150). In this paper we present the main experimental data of the investigations.

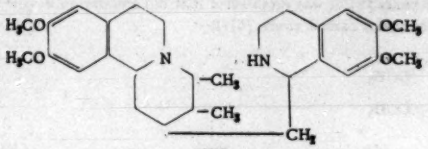
** Deceased.

of the products of destruction of emetine formed mainly by its exhaustive methylation, and a large number of compounds were isolated which were characterized and whose structure was determined. These studies show indisputably that the nonnitrogenous skeleton of emetine has the structure:

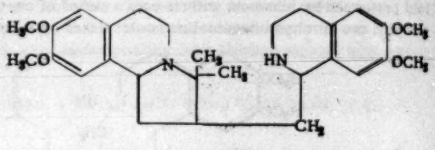


(VI)

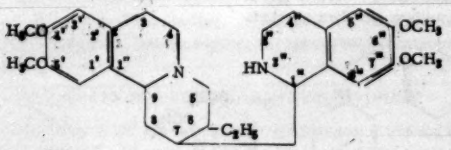
On this basis three possible formulas for the alkaloid can be advanced:



(VII)

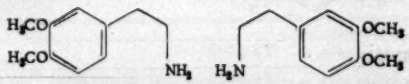


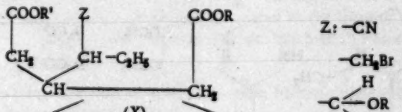
(VIII)

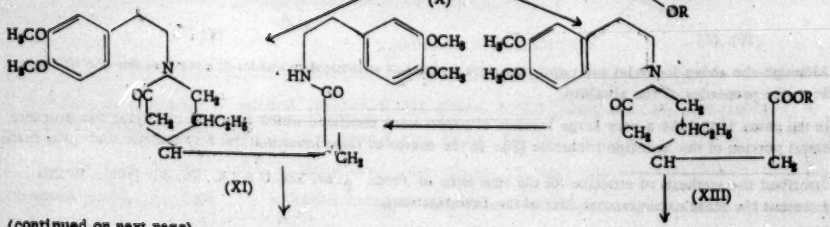


(IX)

Scheme of Emetine Synthesis

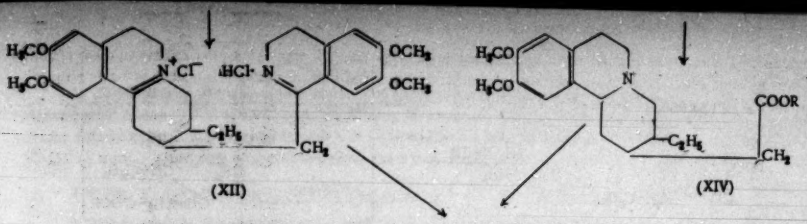






(XI) (XIII)

(continued on next page)



(XII) (XIV)

(IX)

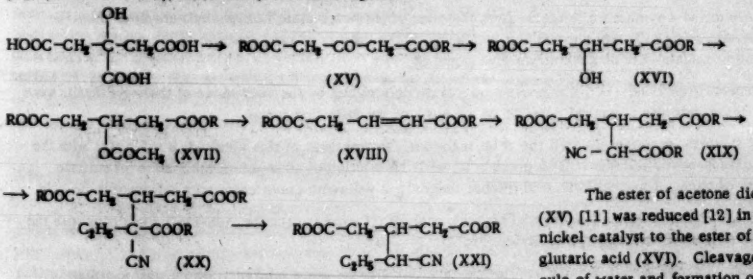
On the basis of our synthetic studies in the field of isoquinoline compounds possessing structures close to those proposed for emetine [9], we arrived at the conclusion that the most probable one was formula (IX). Robinson [10] also reached this conclusion on the basis of his concepts of the structural-genetic relationship of the alkaloids of the isoquinoline group. However, the problem of the structure of emetine could not be considered to be conclusively solved in the absence of a synthesis. This synthesis has now been effected and in this paper we describe our synthesis of emetine.

We had studied several routes to emetine which are characterized by the general scheme set out above.

At the basis of our emetine synthesis lay the idea of utilizing a starting substance in whose structure would previously predominate the whole of the central part of the emetine molecule, i.e., that part most in need of experimental demonstration. The structure of this starting material corresponds to the general formula (X). The presence in the hydrocarbon chain of compound (X) of the requisite and appropriately arranged active groups –COOH, –CN, $-CH(OR)_2$, $-CH_2Br$, enables to be built up, by condensation with homoveratrylamine, the structure of the quinolizine and isoquinoline systems entering into the structure of emetine.

For utilization as starting materials for the central portion of the emetine molecule we synthesized the following compounds: a) the ethyl ester of β-(α'-bromomethoxy)-propylglutaric acid (X) (Z = $-CH_2Br$); b) γ-ethyl-Δ-valerolactone-β-acetic acid; c) the anhydride of β-(α'-diethylacetal)-propylglutaric acid (X) (where Z = $-C(OH)_2$) and d) the ester of β-(α'-cyano)-propylglutaric acid (X) (where Z = –CN).

In this paper we present the synthesis of emetine starting from the ester of β-(α'-cyano)-propylglutaric acid (X), (where Z = –CN), obtained by the following route:

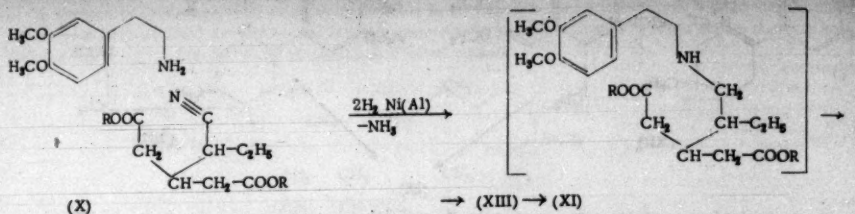


(XV) (XVI) (XVII) (XVIII) (XIX)

(XX) (XXI)

The ester of acetone dicarboxylic acid (XV) [11] was reduced [12] in presence of nickel catalyst to the ester of β-hydroxyglutaric acid (XVI). Cleavage of a molecule of water and formation of the ester of glutaconic acid (XVIII) were effected both by boiling β-hydroxyglutaric acid in benzene and by conversion into the β-acetoxy derivative (XVII) followed by cleavage of a molecule of acetic acid [13]. By condensation with ethylcyanoacetate (XIX) [14] and ethyl iodide in presence of sodium alcoholate there is obtained the ester of β-(α'-cyano-α'-carbethoxy) propylglutaric acid (XX). After saponification with the calculated amount of sodium alcoholate and water followed by acidification and decarboxylation, there is obtained the ester of β-(α'-cyano)-propylglutaric acid (XXI).

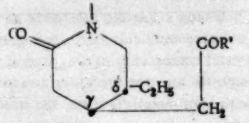
Reductive condensation in presence of nickel or platinum catalyst of the ester of β-(α'-cyano) propylglutaric acid and an excess of homoveratrylamine (route A) leads to addition of the latter to the nitrile group and loss of ammonia [15]. At the same time the resultant secondary amino group enters into reaction with one of the carbalkoxyl groups with formation of an amide bond and closure of the piperidone ring.



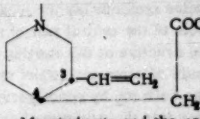
(X) → (XIII) → (XI)

After removal of catalyst and ethyl alcohol, the obtained piperidone derivative (XIII) and excess homoveratrylamine are converted by heating at 180-200° into β"-(3", 4"-dimethoxyphenyl) ethylamide-N-[β'-(3', 4'-dimethoxyphenyl)] ethyl- δ-ethyl-α-piperidone-γ-acetic acid (XI) which comprises a mixture of two stereoisomers: the A-isomer soluble in toluene, and the B-isomer insoluble in toluene.

In this case stereoisomerization similar to that in the quinic alkaloids [16] has taken place, i.e., the presence of A- and B-isomers in compounds (XIII), (XI) and (XII) is the consequence of cis-trans-isomerism at the γ- and δ-carbon atoms:



(XIII), (XI), (XII)



Meroquinene and the corresponding quinine alkaloids

The prepared diamides (XI) are individually subjected to cyclization with phosphorus oxychloride to form the benzquinolizine-isoquinoline derivative (XII). The resultant hydrochlorides of the chloride of 4', 5'-dimethoxy-6-ethyl-7-(1"-methyl-6", 7"-dimethoxy-3", 4"-dihydroisoquinolyl)-3,4,5,6,7,8-hexahydro-9,10-dehydro-(1,2:1', 2')-benzquinolizine (XII) is further hydrogenated in presence of platinum or nickel catalyst, and after appropriate working-up there is obtained 4', 5'-dimethoxy-6-ethyl-7-(1"-methyl-6", 7"-dimethoxy-1", 2", 3", 4"-tetrahydroisoquinolyl)-3,4,5,6,7,8-hexahydro-(1,2:1', 2')-benzquinolizine (IX) – emetine bases.

We also effected a synthesis of emetine from the ester of N-[β-(3,4-dimethoxyphenyl)-ethyl)-β-ethyl-α-piperidone-γ-acetic acid (XIII), an intermediate compound of the product of condensation of the nitrile (X) (Z = –CN) with one molecule of homoveratrylamine (route B).

The prepared compounds (IX), whose structure was predetermined by the very mode of their synthesis, were proved to possess the structure of natural emetine on the basis of the following facts:

1. The synthetic emetines give all the color reactions characteristic of this alkaloid: a red color with the sodium salt of diazobenzene sulfonic acid; a green color with 1% solution of ammonium molybdate in sulfuric acid in presence of traces of hydrochloric acid (Frohde reagent); a yellowish-green color with sulfomolybdic acid.

2. The absorption curve of the prepared hydrochloride of d,l-emetine (m. pt. 145-146°) coincides with the absorption curve of natural emetine hydrochloride (Fig. 1).

3. Oxidation of the prepared bases with iodine gave one and the same substance which was completely identical with the rubremetine, formed by oxidation of natural emetine (Fig. 2). The rubremetine formed by the action of mild oxidizing agents (iron chloride [17], bromine [18], iodine [19], and mercuric acetate [20]) on the natural alkaloid, does not differ from the rubremetine prepared synthetically.

In view of the presence in the structural formula of emetine of four asymmetric carbon atoms (C_β, C_γ, C_δ, C_1') we may assume that the solid and liquid emetines isolated by us comprise a mixture of isomers due to the asymmetry at the C_1' atom in the isoquinoline nucleus and at the C_β atom in the quinolizine nucleus. For the separation of the individual isomers we converted the obtained bases into various salts. From the solid isomer (m. pt. 60-63°) we succeeded in preparing the crystalline camphor-β-sulfonate, from which was isolated the base with m. pt. 71.5-72.5°. The d-tartarate of the latter (m. pt. 159-161.5°), also the base separated therefrom (m. pt. 71.5-72.5°), are completely identical with, respectively, the d-tartrate and the l-emetine of the natural product.

EXPERIMENTAL

1. Ethyl ester of acetone dicarboxylic acid (XV) is prepared by the usual method, e.g. from citric acid which is treated with concentrated sulfuric acid containing 20% sulfur trioxide followed by esterification of the resultant acetone dicarboxylic acid (92% yield) with ethyl alcohol in presence of hydrogen chloride. B. pt. 118-120° (2 mm), 125-127° (5 mm). Yield 45% of theory based on the citric acid.

The methyl ester of acetone dicarboxylic acid has b. pt. 131-135° at 10 mm. Yield 40% of theory.

2. Ethyl ester of β-hydroxyglutaric acid (XVI). 62 g ethyl acetone dicarboxylate in 20 ml absolute alcohol is hydrogenated in presence of 2 g skeletal nickel catalyst at an initial hydrogen pressure of 130 atm and at a temperature of 150° for 4 hours. After cooling, the catalyst is filtered off, the alcohol distilled off in vacuum, and the residue distilled. B. pt. 128-130° (5 mm). Yield 57.8 g or 92.5% of theory.

Methyl ester of β-hydroxyglutaric acid has b. pt. 138-139° at 8 mm. Yield 85% of theory.

3. Ethyl ester of β-acetoxyglutaric acid (XVII). 57.8 g (1 mole) ethyl β-hydroxyglutarate and 37 g (1.3 moles) freshly distilled acetic anhydride are heated for one hour with gentle boiling. The excess of acetic anhydride and acetic acid are distilled off in vacuum, and the residue is distilled. B. pt. 138-140° at 4 mm. Yield 67.2 g or 96.5% of theory.

Methyl ester of β-acetoxyglutaric acid has b. pt. 134-135° at 5 mm. Yield 95% of theory.

4. Ethyl ester of glutaconic acid (XVIII). 30 g (1 mole) ethyl β-acetoxyglutarate is heated with 0.1 g (0.0084 mole) fused potassium acetate until the acetic acid is distilled off, care being taken that the temperature of the vapor does not exceed 135°. At the end of the distillation potassium acetate comes down and the heating is then stopped. The cooled reaction mass is treated with absolute ether for complete removal of the substance from the potassium acetate. The ether is distilled off and the residue redistilled in vacuum. B. pt. 103-105° at 3 mm, 127-129° at 14 mm. Yield 16.9 g or 74.5% of theory. Dilution of the distilled acetic acid with water yields a further 1-1.5 g of glutaconic ester.

The methyl ester of glutaconic acid has b. pt. 94-95° at 2 mm. Yield 71.5%.

5. Ethyl ester of β-(α'-cyano-α'-carbethoxy)-methylglutaric acid (XIX). A mixture of 63 g (1 mole) freshly distilled ethyl glutarate, 88 g (2.3 moles) ethylcyanoacetate, 63 ml absolute ethyl alcohol and 20 drops sodium ethylate solution (the latter prepared from 3.6 g metallic sodium and 40 ml absolute alcohol) is kept at a gentle boil for 12 hours. Maintenance of the necessary alkaline reaction of the solution is ensured by the addition every two hours of 20 drops of sodium ethylate. After cooling, the alcohol is distilled off in vacuum and to the water is added 15 ml water. The separated oil is collected, the aqueous layer extracted with ether (benzene), the ethereal extract combined with the oil and the whole dried with ignited sodium sulfate. After removal of the solvent the residue is distilled in vacuum. B. pt. 167-169° at 3 mm. Yield 85 g or 84% of theory.

The methyl ester of β-(α'-cyano-α'-carbomethoxy)-methylglutaric acid has b. pt. 157-159° at 2 mm, 189-192° at 10 mm. Yield 74.5% of theory.

6. Ethyl ester of β-(α'-cyano-α'-carbethoxy)-propylglutaric acid (XX). To a solution of sodium ethylate prepared from 7.4 g (1.2 moles) metallic sodium and 148 ml absolute alcohol is added a mixture of 83 g (1 mole) ethyl ester of β-(α'-cyano-α'-carbethoxy)-methylglutaric acid and 92 g (2 moles) ethyl iodide. The reaction mass is kept at the boil until the reaction is neutral, which usually requires 3 hours. On cooling, the alcohol is distilled off in vacuum and to the residue is added 20 ml of water. The separated oil is removed, the aqueous layer is extracted with benzene. After the usual working up of the benzene extract (combined with the oil layer) and distillation of the solvent, the residue is distilled in vacuum. B. pt. 169-171° at 3 mm. Yield 82 g or 88.3% of theory.

d_{15}^{20} 1.0947; n_D^{20} 1.4521; MR_D 80.70; calculated 80.85.

3.035 mg substance: 6.545 mg CO_2; 2.080 mg H_2O; 5.945 mg substance: 0.245 ml N_2 (24°, 731 mm). Found %: C 58.81; H 7.66; N 4.5. $C_{16}H_{25}O_6N$. Calculated %: C 58.68; H 7.70; N 4.27.

The methyl ester of β-(α'-cyano-α'-carbethoxy)-propylglutaric acid is prepared similarly, by condensation of methyl glutaconate with methyl ethylcyanoacetate. The yield was lower. B. pt. 150-152° at 1 mm.

d_{15}^{20} 1.825; n_D^{20} 1.4597; MR_D 65.97. $C_{13}H_{19}O_6N$. Calculated: MR_D 65.75.

7. Ethyl ester of β-(α'-cyano)-propylglutaric acid (X, Z = –CN). To a solution of sodium alcoholate prepared from 1.81 g (1 mole) metallic sodium and 40 ml absolute ethyl alcohol is added 25.8 g (1 mole) ethyl ester of β-(α'-cyano-α'-carbethoxy)-propylglutaric acid (XX). The reaction mass turns yellow and thickens. Addition is then made of 1.42 g (1 mole) water and the mass left for 12 hours and then heated for an hour at the boil. The excess of alcohol is distilled off in vacuum and the residue dissolved in 15 ml of water. The solution is extracted with ether to remove the unsaponified tricarboxylic ester and then cooled before acidifying with hydrochloric acid. An oil separates and is carefully extracted with ether. After removing the ether from the dried extract, the residue is heated in a vacuum (15 mm) at 170-180° for one hour. The residue is cooled and dissolved in ether, and the solution well washed with sodium bicarbonate solution. After drying with magnesium sulfate, the ether is distilled off and the residue distilled in vacuum. B. pt. 139-140° at 2.5 mm. Yield 6 g or 30 % of theory.

d_{4}^{20} 1.0535; n_{D}^{20} 1.4519; MR_D 65.32; calculated 65.35.

3.320 mg substance: 7.430 mg CO_2; 2.460 mg H_2O. 3.170 mg substance: 7.130 mg CO_2; 2.310 mg H_2O.
5.110 mg substance: 0.254 ml N_2 (23°, 719 mm). 5.480 mg substance: 0.263 ml N_2 (22°, 728 mm).
Found %: C 61.03, 61.34; H 8.29, 8.15; N 5.45, 5.31. $C_{12}H_{21}O_4N$. Calculated %: C 61.14; H 8.29; N 5.48.

8. β"-(3", 4"-Dimethoxyphenyl)-ethylamide-N-[β'-(3',4'-dimethoxyphenyl)]-ethyl-δ-ethyl-α-piperidone-γ-acetic acid – diamide (XI). A mixture of 5.2 g (1 mole) ethyl ester of β-(α'-cyano)-propylglutaric acid, 24 g (6.5 moles) homoveratrylamine, 8 g skeletal nickel catalyst and 15 ml absolute ethyl alcohol is heated in an autoclave at 110-115° and an initial hydrogen pressure of 130 atms for two hours. After cooling, the catalyst is filtered off. The alcohol is distilled off in vacuum, and the residue heated on an oil bath at 180-200° for three hours. The cooled reaction mass is rapidly and thoroughly washed with excess (200-300 ml) absolute ether in order to remove homoveratrylamine. The residue after removing the ether solution is a yellow, viscous oil soluble in alcohol and chloroform, insoluble in water, ether and benzene. It is a mixture of stereoisomeric diamides. Yield 9.0 g or 86% of theory.

7.450 mg substance: 0.358 ml N_2 (24°, 735 mm). Found %: N 5.34. $C_{38}H_{58}O_6N_4$. Calculated %: N 5.59.

The obtained mixture was resolved with the help of absolute toluene into two fractions: 3.2 g of isomer A, soluble in toluene, and 5.8 g of isomer B, insoluble in toluene. Further transformations were performed separately with each isomer.

9. Hydrochloride of 4', 5'-dimethoxy-6-ethyl-7-(1"-methyl-6", 7"-dimethoxy-3", 4"-dihydroisoquinolyl)-3, 4, 5, 6, 7, 8-hexahydro-9, 10-dehydro-(1,2:1',2')-benzquinolizine chloride (XII).

a) A mixture of 3.2 g isomer A of β"-(3", 4"-dimethoxyphenyl)-ethylamide-N-(β'-(3', 4'-dimethoxyphenyl-ethyl)-δ- ethyl-α-piperidone- γ -acetic acid, dissolved in 40 ml absolute toluene, and 25 ml freshly distilled phosphorus oxychloride is heated for an hour at a gentle boil. The toluene and excess phosphorus oxychloride are distilled off in vacuum. The residue is washed several times with absolute alcohol and then dissolved in 8 ml of 6 % hydrochloric acid. The solution is evaporated in vacuum to give 3.5 g of red-brown oil readily soluble in water, alcohol and chloroform , insoluble in ether and benzene.

b) A mixture of 5.8 g of isomer B of β"-(3", 4"-dimethoxyphenyl)-ethylamide-N-[β'-(3', 4'-dimethoxyphenyl)-ethyl]- δ-ethyl-α-piperidone-γ-acetic acid, suspended in 40 ml toluene, and 4.5 ml freshly distilled phosphorus oxychloride is heated for an hour at a gentle boil. Further treatment was as for isomer A. There was obtained 6.2 g red-brown oil. The latter was characterized by preparation of the corresponding hydroiodide of 4', 5'-dimethoxy-6-ethyl-7-(1"-methyl-6", 7"-dimethoxy-3", 4"-dihydroisoquinolyl)-3,4,5,6,7,8-hexahydro-9,10-dehydro-(1',2':1,2)-benzquinolizine iodide. To the aqueous solution of hydrochloride of the chloride (XII) is added an aqueous solution of sodium iodide until precipitation is complete. The iodide is extracted with chloroform and the extract dried with ignited magnesium sulfate. Distillation of the solvent leaves a yellow residue. The iodide is purified by dissolving in alcohol and precipitating with ether. The compound is slightly hygroscopic. After drying in a vacuum desiccator the m. pt. is 257-258°. Readily soluble in alcohol and chloroform, sparingly soluble in water, insoluble in ether and benzene.

3.150 mg substance: 5.510 mg CO_2; 1.620 mg H_2O. 3.255 mg substance: 5.710 mg CO_2; 1.660 mg H_2O.
8.380 mg substance: 0.314 ml N_2 (24°, 723.3 mm). Found %: C 47.71, 47.84; H 5.75, 5.71; N 4.09.
$C_{29}H_{39}O_4N_2I_3$. Calculated %: C 47.52; H 5.23; N 3.82.

10. 4', 5'-Dimethoxy-6-ethyl-7-(1"-methyl-6",7"-dimethoxy-1", 2", 3", 4"-tetrahydroisoquinolyl)-3,4,5, 6, 7, 8, hexahydro-1,2:1', 2'-benzquinolizine – emetine bases (IX).

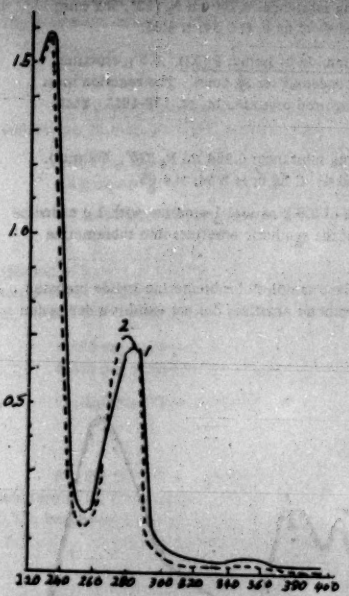


Fig. 1.
1 – Hydrochloride of natural emetine;
2 – hydrochloride of synthetic emetine.

a) 3.5 g of hydrochloride of the chloride (XII), prepared from the A isomer (XI), is treated in 10 ml absolute alcohol with alcoholic ammonia solution. The resultant precipitate is filtered, and the alcoholic filtrate is charged into an autoclave where it is hydrogenated in presence of 8 g skeletal nickel catalyst at 70-80° and an initial hydrogen pressure of 130 atm. for two hours. After cooling, the catalyst is removed, the alcohol distilled off in vacuum and the residue dissolved in 8 ml water. The aqueous solution is treated with ammonia while being cooled, and the separated oil is extracted with ether. The extract is washed with 5% alkali solution and dried with potassium carbonate. After removing the ether, a light-yellow oil remains. Yield 1.7 g or 55.5% of theory.

6.060 mg substance: 0.323 ml N_2 (22°, 741 mm). Found %: N 6.01. $C_{29}H_{40}O_4N_2$. Calculated %: N 5.89.

b) In a similar manner, 6.2 g of the hydrochloride of the chloride (XII), prepared from isomer B (XI), is converted (after distilling off the ether) into a yellow, amorphous substance with m. pt. 60-63°. Yield 1.0 g or 18.4% of theory.

When using platinum catalyst this process proceeds in the following manner: 4 g hydrochloride of chloride (XII), prepared from isomer B (XI), in 15 ml alcohol is hydrogenated in presence of 0.4 g platinum oxide at 1.5-2 atm. After 0.5 mole hydrogen has been taken up, which requires 30 minutes, the hydrogenation comes to a stop. The inactivated catalyst is filtered off, 0.2 g fresh platinum oxide is added, and hydrogenation is resumed at 130 atm., 1.5 moles hydrogen being then absorbed in 10-15 minutes. The solution, dark-red in color prior to hydrogenation, is light-yellow. Further treatment is as above. There is obtained a white, amorphous substance which turned yellow in the light. Yield 1.4 g or 40% of theory.

5.235 mg substance: 0.284 ml N_2 (25°, 740 mm). Found %: N 6.04. $C_{29}H_{40}O_4N_2$. Calculated %: N 5.89.

11. Emetine hydrochloride. a) It was not possible to isolate the crystalline hydrochloride of the emetine prepared from isomer A (XI).

b) The ethereal solution of the emetine base prepared from isomer B (XI), was saturated with an ethereal solution of hydrogen chloride to give a white powder with m. pt. 145-146° (beings to change at 100-102°). The substance is readily soluble in water and alcohol, insoluble in ether and benzene; it is hygroscopic. Prior to each analysis the preparation was dried in vacuum at 110° for 1½ hours.

3.110 mg substance: 7.205 mg CO_2; 2.140 mg H_2O. 4.845 mg substance: 0.225 ml N_2 (22°, 735 mm). 5.320 mg substance: 2.695 mg AgCl. Found %: C 63.18; H 7.70; N 5.2; Cl 12.55.

$C_{29}H_{40}O_4N_2 \cdot 2HCl$. Calculated %: C 62.89; H 7.48; N 5.06; Cl 12.83.

The absorption spectrum of the hydrochloride of synthetic emetine is identical with that of the hydrochloride of natural emetine (Fig. 1).

12. Rubremetine iodide. a) Oxidation of the synthetic emetine base obtained from isomer A diamide (XI). 0.5 g base, 20 ml ethyl alcohol and 1 g iodine are heated for 3 hours on the water bath and for 45 minutes on the oil bath at 140-145°. The reaction mass, after cooling, is poured into sodium becarbonate solution. A brown precipitate is formed. This is drained, washed with water and recrystallized from a mixture of acetone and water. M.p. 178.5-181°. Yield 0.08 g or 12.8% of theory.

3.150 mg substance: 6.685 mg CO_2; 1.600 mg H_2O. 6.060 mg substance: 0.240 ml N_2 (23°, 752 mm). Found %: C 57.88; H 5.68; N 4.52. $C_{29}H_{33}O_4N_2I$. Calculated %: C 58.0; H 5.54; N 4.65.

b) Oxidation of synthetic emetine base prepared from the diamide of isomer B (XI). 0.5 g emetine base, 20 ml ethyl alcohol and 1 g iodine are heated under a reflux condenser for 3½ hours. The reaction mass is treated as in a). Rubremetine iodide separates in the form of orange-red crystals. M. pt. 178-181°. Yield 0.12 g, 19.2% of theory.

3.185 mg substance: 6.765 mg CO_2; 1.555 mg H_2O. 6.335 mg substance: 0.264 ml N_2 (25°, 752 mm). Found %: C 57.93; H 5.46; N 4.72. $C_{29}H_{33}O_4N_2I$. Calculated %: C 58.0; H 5.54; N 4.65.

c) Oxidation of natural emetine base. Heating of a mixture of 0.5 g natural l-emetine with 1 g of iodine in alcoholic solution under the conditions described for conversion of the synthetic emetines into rubremetine iodide gives 0.15 g rubremetine iodide (24% of theory).

The prepared rubremetine iodide melts at 177-179°. The mixed samples of rubremetine iodide prepared from natural emetine with the rubremetine iodides prepared from synthetic emetines did not exhibit a depression. The absorption spectra of the prepared rubremetine iodides coincide completely (Fig. 2).

13. Camphor-β-sulfonate of natural l-emetine. 0.177 g (1 mole) natural l-emetine base is dissolved in absolute alcohol and addition is made of 0.170 g (2 moles) of d,l-camphor-β-sulfonic acid and a few drops of absolute ether. A precipitate comes down on standing and is filtered off and washed with absolute alcohol and ether. There is obtained 0.1723 g camphor-β-sulfonate of l-emetine with m. pt. 210-213°. After recrystallization from absolute alcohol the yield is 0.0943 g or 27.1% of theory. M. pt. 222-223°.

3.150 mg substance: 7.210 mg CO_2; 2.075 mg H_2O. 3.050 mg substance: 6.950 mg CO_2; 2.085 mg H_2O. 5.565 mg substance: 0.147 ml N_2 (24°, 746 mm). 5.295 mg substance: 0.150 ml N_2 (23°, 743 mm). Found %: C 62.42, 62.14; H 7.37, 7.65; N 2.98, 3.19. $C_{29}H_{40}O_4N_2 \cdot 2C_{10}H_{16}O_4S$. Calculated %: C 62.25; H 7.68; N 2.96.

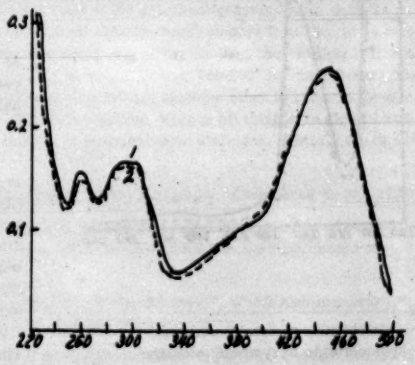


Fig. 2.
1 – Rubremetine iodide prepared from natural emetine; 2 – rebremetine iodide prepared from synthetic emetine.

14. Camphor-β-sulfonate of synthetic emetine. a) 1.033 g (1 mole) emetine base with m. pt. 60-63°, prepared from B-isomer diamide (XI), is dissolved in 5 ml absolute alcohol and addition is made of 0.996 g (2 moles) d,l-camphor-β-sulfonic acid. On introducing a seed of the camphor-β-sulfonate of natural emetine, a precipitate gradually comes down. The salt is filtered off and washed with absolute alcohol and ether. There is obtained 0.2392 g (12% of the theoretical yield) of emetine camphor-β-sulfonate with m. pt. 225-227.5°. Recrystallization from absolute alcohol gave 0.212 g (10.4% of the theoretical yield). M. pt. 238.5-240°.

3.005 mg substance: 6.870 mg CO_2; 2.040 mg H_2O. 2.990 mg substance: 6.850 mg CO_2; 2.070 mg H_2O. 5.055 mg substance: 0.119 ml N_2 (22°, 748 mm). 7.20 mg substance: 0.171 ml N_2 (25°, 745.4 mm). Found %: C 62.35, 62.48; H 7.59, 7.75; N 2.68, 2.67. $C_{29}H_{40}O_4N_2 \cdot 2C_{10}H_{16}O_4S$. Calculated %: C 62.25; H 7.68; N 2.96.

b) The emetine base prepared from isomer A diamide (XI) does not form crystalline products with camphor-β-sulfonic acid. A substance identical with that described above could only be isolated in a small yield.

15. Isolation of emetine base from emetine camphor-β-sulfonate. a) Synthetic emetine. 0.158 g camphor-β-sulfonate of synthetic emetine with m. pt. 238.5-240° is dissolved in 12 ml water and treated with 10% sodium hydroxide solution. The resultant precipitate of emetine base is filtered and washed with water. M. pt. 71.5-72.5°. Yield 0.056 g, 69.7% of theory. Emetine base was obtained in the form of a white amorphous powder,

readily soluble in methyl and ethyl alcohols, ether, acetone and chloroform, less easily soluble in carbon tetrachloride, petroleum, ether and benzene, sparingly soluble in water.

3.010 mg substance: 7.980 mg CO_2; 2.120 mg H_2O. Found %: C 72.30; H 7.88. $C_{29}H_{40}O_4N_2$. Calculated %: C 72.45; H 8.39.

b) l-Emetine (natural). From 0.15 g natural emetine camphor-β-sulfonate is obtained l-emetine base with m. pt. 71.5-72.5°. Yield 0.05 g, 65.0% of theory.

3.025 mg substance: 8.010 mg CO_2; 2.100 mg H_2O. Found %: C 72.33; H 7.78. $C_{29}H_{40}O_4N_2$. Calculated %: C 72.45; H 8.39.

No depression was observed in a mixed melting point determination on synthetic and natural emetines.

16. Emetine hydrochloride. To an ethereal solution of synthetic emetine base is added a saturated ethereal solution of hydrogen chloride. The resultant precipitate of emetine hydrochloride is washed several times with absolute ether. It forms a white powder with m. pt. 243-255°. The hydrochloride prepared from natural emetine has m. pt. 235-255°. Prior to each analysis the preparation is dried in vacuum at 110° for 1½ hours.

3.080 mg substance: 7.110 mg CO_2; 2.045 mg H_2O. 6.000 mg substance; 0.289 ml N_2 (23°, 727 mm). 5.950 mg substance: 3.025 mg AgCl. Found %: C 62.96; H 7.43; N 5.31; Cl 12.58.

$C_{29}H_{40}O_4N_2 \cdot 2HCl$. Calculated %: C 62.89; H 7.48; N 5.06; Cl 12.83.

SUMMARY

For the first time a complete synthesis of the alkaloid, emetine, has been realized. It has confirmed its structure as 4', 5'-dimethoxy-6-ethyl-7-(1"-methyl-6", 7"-dimethoxy-1", 2", 3", 4"-tetrahydroisoquinolyl)-3,4,5, 6,7,8,-hexahydro-1,2:1',2'-benzquinolizine.

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Determination of the Mixed Sulfates of the Alkali Elements and Ammonium.

(Viktor I. Spitsyn and M. A. Meerov. p. 1327)

Crystals of cesium-ammonium sulfate (X 10).

REACTIONS OF TRIARYLBROMOMETHANES WITH (ALKYL)PYROCATECHOL ESTERS OF PHOSPHOROUS ACID

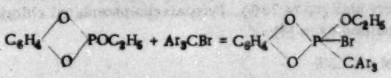
A. E. Arbuzov and F. G. Valitova

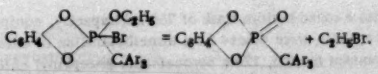
Reactions of the ethyl ester of pyrocatechol phosphorous acid with triarylbromomethanes were studied. The interaction of these compounds gives pyrocatechol triarylmethylphosphinates. On hydrolysis of the latter with dilute hydrochloric acid, pyrocatechol and triarylmethylphosphinic acids are obtained.

The present study deals with the reactions of mixed esters of phosphorous acid, of the type

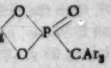
POR (where R is C_2H_5), with triarylbromomethanes.

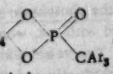
The reaction between (ethyl)pyrocatechol ester of phosphorous acid and triarylbromomethanes should proceed, by analogy with alkyl phosphites, according to the reactions:





It has been shown experimentally that the reaction proceeds indeed according to the equations indicated. Thus, for example, when a mixture of a triarylbromomethane and (ethyl)pyrocatechyl phosphite is heated, evolution of ethyl bromide takes place and a crystalline substance is formed, which is the pyrocatechol ester of triarylmethyl-phosphinic acid. To determine the structure of the obtained compounds the latter were hydrolyzed with dilute hydrochloric acid by heating at 180 to 200° in sealed tubes. The products of hydrolysis were pyrocatechol and triarylmethylphosphinic acids.

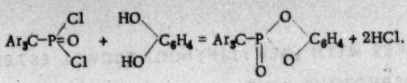
The obtained esters, of the type  , are very stable to atmospheric humidity. Stored in air for a month, they remained completely unaltered; on treatment with water, even when boiled in water, there was no change whatsoever.

Pyrocatechol esters of triarylmethylphosphinic acids,  , are colorless crystalline substances, insoluble in water, alcohol, ether, and difficultly soluble in benzene.

As a result of our research, by reaction of (ethyl)pyrocatechyl phosphite with triphenylbromomethane, diphenyl-biphenylbromomethane, phenyldi(biphenyl)bromomethane, phenylxanthyl bromide, and diphenyl-α-naphthylbromomethane, the respective pyrocatechyl triarylmethylphosphinates were prepared, whereas their hydrolysis gave the corresponding triarylmethylphosphinic acids, except phenylxanthylphosphinic acid. The formulas and melting points of the esters and their product of hydrolysis are given in the table.

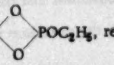
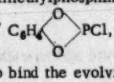
Two esters, with diphenylbiphenylmethyl and phenylbiphenylmethyl radicals, were obtained by A. E. Arbuzov and Nikonorov [1] by another method, in their research on the properties of analogs of the chloride

of Boyd's acid (triarylmethanephosphorylchloride) by reaction of pyrocatechol with triphenylmethyl dichlorophosphine oxide, according to the following equation:

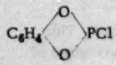


The esters, obtained by us by the method described above, were equivalent in their physicochemical properties to those obtained by Arbuzov and Nikonorov.

Thus, the obtained derivatives of pyrocatechol esters of phosphorous acid and the study of their properties and behavior led to compounds that are similar in structure to compounds prepared from Boyd's acid chlorides, confirming again the viewpoints of A.E. and B. A. Arbuzov [2] on the structure of Boyd's acid chloride as a compound of pentavalent phosphorus.

The (ethyl)pyrocatechol ester of phosphorous acid,  , required for the preparation of pyrocatechol esters of triarylmethylphosphinic acids, was obtained by reaction of absolute alcohol with pyrocatecholphosphinyl chloride,  , according to the method of Milobendzki and Sachanowsky [3], except that pyridine, used to bind the evolving hydrogen chloride, was replaced by dimethylaniline. It should be mentioned that the yield of ester by this method is very high (up to 70%). Pyrocatecholphosphinyl chloride was prepared according to the method of Anschutz as modified by us [4].

EXPERIMENTAL

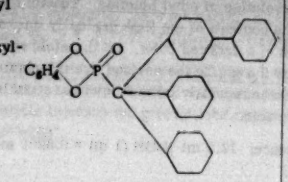
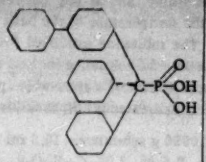
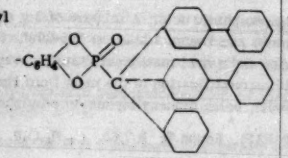
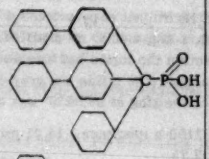
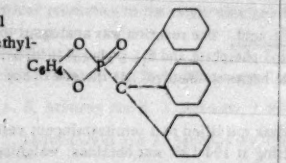
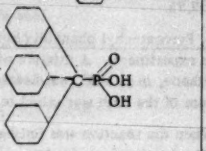
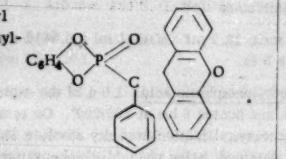
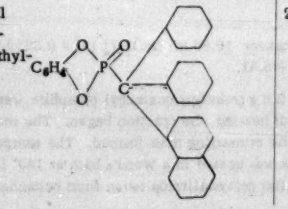
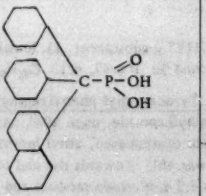
1. Preparation of (ethyl)pyrocatechyl phosphite. Into a round-bottom flask of 750 ml capacity, equipped with a mechanical stirrer, a dropping funnel, and reflux condenser, were placed 84 g dimethylaniline in ether solution and 31.6 g absolute alcohol. With the stirrer in constant motion, 120 g pyrocatecholphosphinyl chloride,  , dissolved in ether, was added from the dropping funnel. When half of the required quantity had been added, two layers formed in the reactor: a clear bottom layer and a turbid upper layer. Toward the end of the reaction a white precipitate of dimethylaniline hydrochloride separated. When the reaction had come to an end the precipitate was filtered off and washed with dry ether. The filtrate and ether washings were distilled; first the ether was driven off, then the (ethyl)pyrocatechyl phosphite was distilled in vacuo. The ester was purified by threefold redistillation in vacuo, using a three-bulb fractionating column. A fraction boiling at 99-100° at 17 mm was obtained, weighing 88 g. The yield of ester was 69.6%, based on the acid chloride.

2. Pyrocatechyl triphenylmethylphosphinic acid. Into a flask of 50 ml capacity, provided with a discharge tube, extending into the flask, cooled with ice, were placed 7 g (ethyl)pyrocatechyl phosphorous acid and 12.3 g triphenylbromomethane, m.p. 152°. The vessel was heated in a Wood's metal bath. At approximately 100° triphenylmethane began to dissolve gradually and at 150° the reaction began with evolution of vapors, which condensed in the cooled flask. When the reaction was finished, the flask was heated for 2 minutes longer at a bath temperature of 160°. The reaction product was a semitranslucent, viscous, slightly yellow mass, which solidified completely on standing overnight. The obtained substance did not dissolve in alcohol, ether, acetone and was difficultly soluble in benzene. A snow-white powder precipitates as a rule from the benzene solution; however, sometimes regularly shaped crystals separate, most frequently as fine oblong platelets. The yield is almost quantitative. After two-fold recrystallization from dry benzene the substance melts at 186°. The m.p. did not change on subsequent recrystallization. Yield, 10 g.

The obtained substance is pyrocatechyl triphenylmethylphosphinic acid.

0.1165 g substance: 16.8 ml NaOH. 0.1158 g substance: 15.96 ml NaOH. (1 ml NaOH= 0.5618 ml P). Found %: P 8.10, 7.74, $C_{25}H_{19}O_3P$. Calculated %: P 7.78.

The liquid which condensed on the walls of the cooled flask was found to be ethyl bromide. Total evolved, 2.9 g ethyl bromide.

No.	Name and formula	M.p.	Products of hydrolysis	M.p.
1	Pyrocatechyl diphenylbiphenylmethylphosphinic acid 	167-168°	Diphenylbiphenylmethylphosphinic acid 	269-270°
2	Pyrocatechyl phenyldibiphenylmethylphosphinic acid 	194-195	Phenyldi(biphenyl)methylphosphinic acid 	160-162
3	Pyrocatechyl triphenylmethylphosphinic acid 	186	Triphenylmethylphosphinic acid 	277.5-279
4	Pyrocatechyl phenylxanthylphosphinic acid 	192-193	Not obtained	
5	Pyrocatechyl diphenyl-α-naphthylmethylphosphinic acid 	235-237	Diphenyl-α-naphthylmethylphosphinic acid 	260-263

3. Hydrolysis of pyrocatechyl triphenylmethylphosphinic acid. Pyrocatechyl triphenylmethylphosphinic acid (5 g) was sealed in a tube with 5 ml HCl (sp.gr. 1.13) and 25 ml distilled water. The tube was heated 6 hours at 180°. On cooling, the liquid assumed a light brown coloration, and long needle-shaped crystals and a hard mass, gray in color, separated. The crystals and the mass were filtered off and were recrystallized from absolute alcohol. After five recrystallizations a substance melting at 277.5-279° was obtained as filiform crystals of triphenylmethyl phosphinic acid.

0.1388 g substance: 20.8 ml NaOH. 0.1275 g substance: 19.21 ml NaOH. (1 ml = 0.6239 mg P).
Found %: P 9.34, 9.40. $C_{19}H_{17}O_3P$. Calculated %: P 9.56.

The crystals were sucked off and the filtrate was extracted with ether. On evaporation of the ether, the crystals remaining in the dish were purified by recrystallization from benzene. The obtained substance had the odor of pyrocatechol and melted at 98°, which is close to the m.p. of pyrocatechol (100°).

4. Pyrocatechyl diphenylbiphenylmethylphosphinic acid. A mixture of 2 g (ethyl)pyrocatechyl phosphite and 4.5 g diphenylbiphenylbromomethane, m.p. 125-127°, was heated in a Wood's bath. At 120° the bromide began to dissolve, and at 155° the reaction began with the evolution of ethyl bromide. Toward the end of the reaction the temperature of the bath was raised to 170°. The contents of the flask gradually thickened and discolored. The substance solidified overnight to a glassy mass of a dark-red color. On threefold recrystallization from benzene, the substance melted at 167-168° and weighed 2.5 g. To the unaided eye the obtained substance had the appearance of a snow-white powder; under a microscope regularly formed colorless crystals were seen. The substance is pyrocatechyl diphenylbiphenylmethyiphosphinic acid.

0.0996 g substance: 10.3 ml NaOH. 0.1087 g substance: 12.2 ml NaOH (1 ml = 0.6239 mg P). Found %: P 6.45, 7.00. $C_{31}H_{25}O_3P$. Calculated %: P 6.54.

5. Hydrolysis of pyrocatechyl diphenylbiphenylmethylphosphinic acid. A mixture of 2 g of the ester, 5 ml HCl (sp. g. 1.13), and 25 ml distilled water was sealed in a tube and heated 5 hours at 190-200°. On termination of the reaction the liquid had assumed a dark-brown coloration and a hard mass precipitated, covered with a lustrous lacquer (the inside was gray-colored). After fourfold recrystallization of the mass from absolute alcohol, a substance melting at 269-270° was obtained as a white powder, being diphenylbiphenylmethylphosphinic acid.

0.1150 g substance: 14.01 ml NaOH (1 ml = 0.6239 mg P). Found %: P 7.60. $C_{25}H_{21}O_3P$. Calculated %: P 7.75.

6. Pyrocatechyl phenyldi-(biphenyl)methylphosphinic acid. The reaction was analogous to that in the preceding experiments. A mixture of 2 g (ethyl) pyrocatechyl phosphite and 5.1 g phenyldi(biphenyl)methylbromomethane, m.p. 144°, was heated. At 130° the bromide began to dissolve. At the end of the reaction the temperature of the bath was raised to 175°.

When the reaction was finished the contents of the flask solidified to a semitranslucent yellowish mass. Recrystallized twice from dry benzene, a white powder melting at 194-195° was obtained, weighing 1.9 g. The substance is pyrocatechyl phenyldi-(biphenyl)methylphosphinic acid.

0.1243 g substance: 11.5 ml NaOH. 0.1312 g substance: 12.7 ml NaOH (1 ml = 0.5618 mg P). Found %: P 5.19, 5.43. $C_{37}H_{27}O_3P$. Calculated %: P 5.61.

7. Hydrolysis of pyrocatechyl phenyldi-(biphenyl)methylphosphinic acid. 1.3 g of the ester and 5 ml HCl (sp. gr. 1.13), in 25 ml distilled water were sealed in a tube and heated 6 hrs at 190-200°. On termination of the reaction, the separating dark-gray hard mass was purified by recrystallization from dry absolute alcohol. After four recrystallizations, a substance melting at 160-162° was obtained, being phenyldi-(biphenyl)methylphosphinic acid.

0.1127 g substance: 11.70 ml NaOH, 0.1099 g substance: 10.80 ml NaOH (1 ml = 0.6239 mg P). Found %: P 6.47, 6.13. $C_{31}H_{25}O_3P$. Calculated %: P 6.51.

8. Pyrocatechyl phenylxanthylphosphinic acid. To 2.9 g (ethyl)pyrocatechyl phosphite was added 5 g phenylxanthylbromide, m.p. 227°. After 3 to 4 min, without heating, the reaction began. The red color of the bromide disappeared, ethyl bromide evolved, and a white crystalline mass formed. The temperature within the flask was 45°. Towards the end of the reaction the flask was heated in a Wood's bath at 140° for 10 min. This gave 6.2 g of crude product and 1 g ethyl bromide. After recrystallizing twice from benzene, a snow white powder, m.p. 192-193°, was obtained.

Analysis showed that the product is pyrocatechyl phenylxanthylphosphinic acid.

0.1432 g usbstance: 19.9 ml NaOH. 0.2194 g substance: 27.9 ml NaOH (1 ml = 0.5618 mg P). Found %: P 7.80, 7.14. $C_{25}H_{17}O_4P$. Calculated %: P 7.52.

9. Hydrolysis of pyrocatechyl phenylxanthylphosphinic acid with HCl, under conditions analogous to the preceding experiments, did not give the corresponding phenylxanthylphosphinic acid.

10. Pyrocatechyl diphenyl-α-naphthylmethylphosphinic acid. A mixture of 2 g (ethyl)pyrocatechyl phosphite and 3.9 g diphenyl-α-naphthylbromomethane was heated at 170-180°. The reaction proceeded with evolution of ethyl bromide, as before. Toward the end of the reaction the temperature of the bath was raised to 200°. The obtained hard mass gave after twofold recrystallization from benzene a white powder, m.p. 235-237°. Ethyl bromide, 0.8 g.

Analysis gave values corresponding to pyrocatechyl diphenyl-α-naphthylmethylphosphinic acid.

0.1441 g substance: 16.9 ml NaOH. 0.1156 g substance: 13.89 ml NaOH (1 ml = 0.6048 mg P). Found %: P 7.08, 7.26. $C_{29}H_{21}O_3P$. Calculated %: P 6.91.

11. Hydrolysis of pyrocatechyl diphenyl- α-naphthylmethylphosphinic acid. 1.5 g of the ester and 5 ml HCl (sp. gr. 1.13) in 25 ml distilled water was sealed in a tube and heated 5 hours at 200-210°. On termination of the hydrolytic reaction the precipitated mass was recrystallized from absolute alcohol. The obtained crystals melted at 260-263°.

SUMMARY

1. By reaction of (ethyl)pyrocatechyl phosphite with triphenylbromomethane, diphenylbiphenylbromethane, phenyldi-(biphenyl)bromomethane, phenylxanthylbromide, and diphenyl-α-naphthyl bromomethane, the respective pyrocatechol esters of triarylmethylphosphinic acids were obtained.

2. Hydrolysis of pyrocatechol esters of triarylmethylphosphinic acids gives the corresponding triarylmethylphosphinic acids.

3. Pyrocatechyl triarylmethylphosphinic acids, obtained as indicated above, are equivalent in their physicochemical properties to the esters obtained from chlorides of Boyd's acid.

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Kazan Institute of Chemical Technology

PHYSICOCHEMICAL ANALYSIS OF SYSTEMS OF MERCURIC HALIDES AND HALIDES OF AMMONIA AND THE ALKALI METALS

I. FUSION OF THE $HgCl_2$–MeCl SYSTEM

I. N. Belyaev and K. E. Mironov

All of the known compounds of $HgHal_2$ and MeHal* were prepared by methods which used water or other solvent solutions of mercury salts [1-4]. Only a few of those reported melted without decomposition; the others as a rule, decomposed into the constituent components on reaching the melting point temperature.

The best known and most stable types of complex compounds of mercuric halides in aqueous media are $Me_2[HgHal_4]$, which often crystallize with several equivalents of water of crystallization [1,2-4]. Compounds of the type $Me[HgHal_3]$ exist with and without water of crystallization. According to Weinland [4], the mercuric salts gave the most abundant series of multinuclear salts with the ratios of $HgHal_2$: MeHal equal to 2:1, 3:2, and 5:1, where the last ratio was for the cations with the largest volumes: ammonium, rubidium, and cesium. The increase in amount of double compounds as a function of the increase in the radius of Me, which were obtained synthetically, can clearly be seen from the reference book [3]. In B. V. Nekrasov's book [5], it is stated that salt types "correspond to the general formulas of $Me[EHal_3]$ to $Me_4[EHal_6]$" and that the tendency of complex formation of mercury and cadmium increases in the order Cl–Br–I.

There was no reference or statement, in the available literature, to any physico-chemical methods of analysis for the study of $HgHal_2$–MeHal systems in the absence of solvents. In the investigations of Beckman [6], on determination of the molecular weights of sodium, potassium, ammonium, rubidium, cesium, and several other metallic chlorides in molten $HgCl_2$, and also that of Guinchant [7] on determination of the potassium, ammonium and other metallic bromides, the amount of MeHal was not greater than 2-7 mole %. The work of Foote and Martin [8], on the electroconductivity of mixtures of $HgCl_2$ and MeCl, when compared by them with the data of Beckman, led to the advancement of certain ideas of the composition of the complex ions in the melts, even though the amount of MeCl did not exceed 3 mole %. Authentic determinations of salts and ions in melts could not be made on the basis of these reports. In view of the above, it appeared to be of considerable interest to study the reaction of mercuric halides with alkali metal and ammonium halides in melts by means of physico-chemical methods.

EXPERIMENTAL

The $HgCl_2$ was the C.P. grade (Karpov), m.p. 283°. The $HgBr_2$ was synthesized from metallic mercury and bromide [8,10]; m.p. 243°. HgI_2 was prepared from mercuric nitrate II by precipitation with potassium iodide, and was purified by sublimation; m.p. 257°. LiCl was prepared from lithium carbonate by the action of HCl followed by drying in a platinum crucible, m.p. 600°. KCl was the C.P. (Khalbaum) preparation. The rest of the reactants were obtained by the recrystallization of C.P. or analytically pure preparations. The salts were carefully dried before use, and were kept in a desiccator over sulfuric acid during the investigation.

Procedure. The systems were studied by the usual visual-polythermic method, given by A. G. Bergman et al [11]. The pyrex test tube used for the substances was placed in a couple of molybdenum glass. A nichrome-constantan thermocouple was used to measure the temperature. It was calibrated by the melting points of chemically pure: naphthalene –80.1°; tin –231.8°; cadmium –320.9°; zinc –419.4°; and a eutectic mixture of 45% KCl and 55% Na_2SO_4 –517.1°. The melting point and the point of disappearance of the crystals were measured on galvanometer with a mirror scale containing 100 graduations. The first crystals in transparent systems were detected with transmitted light. Reflected light and continuous stirring were used with opaque systems (mercuric iodide).

The experiments were complicated by the comparatively small interval between the melting points and the boiling points of the mercuric halides. In order to determine the liquidus curves, the cooling curves of

* Me = the univalent metals Li, Na, K, Rb, Cs, NH_4. Hal = Cl, Br, I.

certain compositions were partially recorded. During the experiments changes in the substances, visible to the eye, were noted.

TABLE 1

Fusion of the system LiCl–$HgCl_2$

Mole % LiCl	Temp. of appearance of the first crystals	Mole % LiCl	Temp. of appearance of the first crystals
0.0	282.5	1.2	279.5
0.4	282.0	1.8	282.0
0.8	281.0	1.9	297.0

TABLE 2

Fusion of the system NaCl–$HgCl_2$

No.	Mole % NaCl	Temp. of appearance of the first crystals	No.	Mole % NaCl	Temp. of appearance of the first crystals
1	0.0	283.0	8	16.0	268.5
2	5.0	279.0	9	18.0	276.0
3	10.0	271.5	10	18.9	292.5
4	11.5	270.0	11	20.0	303.0
5	13.0	267.5	12	21.5	309.0
6	14.5	267.5	13	23.0	Melts boiled at 312°; the NaCl did not dissolve.
7	15.2	268.0	–	–	–

NOTES. 1) Eutectic 14 mole % NaCl, 264°. 2) Transition point, 17.5 mole % NaCl, 272°. 3) Transition point, 19.5 mole % NaCl, 298°.

The Chloride Systems. System $HgCl_2$–LiCl. The experiment with lithium chloride was done with every precaution in view of its strong hygroscopicity. According to Table 1, it is apparent that LiCl can dissolve only in small amounts in $HgCl_2$. The melt boiled vigorously when the composition was 1.9 mole % LiCl; $HgCl_2$ distilled but the lithium chloride did not dissolve. The eutectic point occurred at 278° and 1.6 mole % of LiCl. It is interesting that the boiling point of the mixture (297°) was lower than the boiling point of pure $HgCl_2$ (308°).

System $HgCl_2$–NaCl. The system was studied up to 23 mole % of NaCl. As the liquidus curve shows (Fig. 1, Table 2), one incongruently melting compound, with a decomposition point at 272°, was formed. The eutectic formed by the chemical compounds and $HgCl_2$ contained 14 mole % of NaCl and melted at 264°.

At 298°, starlike crystals formed which were not observed previously. Apparently, these crystals corresponded to another chemical compound. The composition of this compound can only be determined by a detailed study of the cooling curve. Above 298°, crystals of sodium chloride separated from the melt.

System $HgCl_2$–KCl. The experimental results are given in Fig. 1 and Table 3. The liquidus curve of the system, which was studied up to 65 mole % of KCl (the high melting point of the system prevented further study), contained a series of branches corresponding to the crystallization of the incongruously melting compounds with the composition, $HgCl_2$: KCl equal to: 7:1, 3:2, 1:1 and 1:2. At the higher temperatures, the compound (1:2) decomposed and KCl separated from the melt.

In the region of crystallization of $HgCl_2$, a halt was obtained at 209°, corresponding to the compound $7HgCl_2 \cdot KCl$, which is not shown on the liquidus curve.

System $HgCl_2$–NH_4Cl. This system (Fig. 2, Table 4), the most complete of the systems studied, was studied up to 73 mole % of NH_4Cl. The liquidus curve had a series of transition points corresponding to changes in the solid phase. A chemical compound, composition 1:1, m.p. 218°, and giving a maximum (on the curve) at 50 mole % of NH_4Cl, is shown very clearly on the liquidus curve. Three polymorphic transformations for the compound were found on the cooling curve at temperatures of 213, 207, and 203°. It is interesting to point out that analogous polymorphic transformations were discovered by Wells [12] for the compound $HgCl_2$: CsCl, prepared by a synthetic method in several solvents.

In addition to the 1:1 compound there was still a series of transition points on the liquidus curve at 235, 214, and 243°, corresponding to 23.5, 33.5, and 66.6% NH_4Cl.

According to the given heating and cooling curves, these transition points correspond to the compounds $9HgCl_2 \cdot 2NH_4Cl$, $2HgCl_2 \cdot NH_4Cl$, and $HgCl_2 \cdot 4NH_4Cl$.

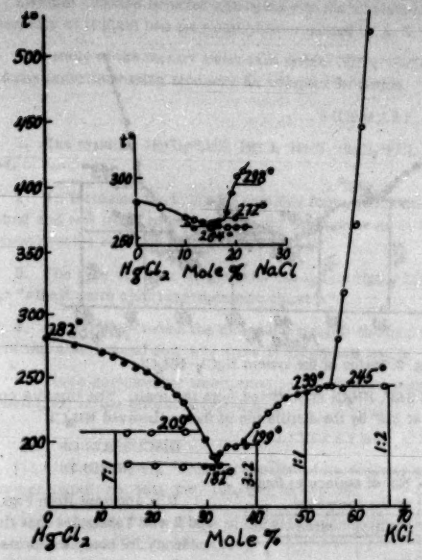

Fig. 1. Fusion of the system $HgCl_2$–NaCl and $HgCl_2$–KCl.

TABLE 4

Fusion of the system NH_4Cl–$HgCl_2$

No.	Mole % NH_4Cl	Temp. of appearance of the first crystals	No.	Mole % NH_4Cl	Temp. of appearance of the first crystals
1	0.0	283.0	18	30.0	228.5
2	2.5	280.0	19	31.5	226.5
3	5.0	275.5	20	32.5	219.5
4	7.5	271.5	21	33.0	214.5
5	10.0	268.0	22	34.0	212.0
6	12.5	263.0	23	35.0	210.0
7	15.0	258.0	24	35.2	209.5
8	16.5	253.0	25	37.0	207.0
9	17.5	249.5	26	37.2	207.0
10	18.0	246.0	27	38.5	205.0
11	19.2	242.0	28	39.0	202.0
12	20.0	240.5	29	40.0	209.5
13	21.0	238.5	30	41.0	209.0
14	22.5	237.0	31	42.0	208.0
15	23.5	235.0	32	42.5	209.5
16	25.0	235.0	33	44.0	212.5
17	27.5	232.0	34	45.0	213.5

(Continued top next page)

TABLE 3

Fusion of the system KCl–$HgCl_2$

No.	Mole % KCl	Temp. of appearance of first crystals
1	0.0	283.0
2	5.0	276.5
3	10.0	271.5
4	12.2	268.0
5	14.5	263.0
6	16.7	259.0
7	18.8	254.5
8	20.7	249.0
9	22.6	244.0
10	24.4	238.0
11	25.6	232.0
12	30.0	203.0
13	31.5	189.0
14	33.0	193.0
15	34.5	197.0
16	36.0	198.0
17	37.5	201.0
18	40.0	213.0
19	42.5	222.0
20	44.0	229.0
21	46.0	234.0
22	48.5	237.0
23	50.0	239.0
24	52.5	242.0
25	54.4	244.0
26	55.0	245.0
27	57.5	318.0
28	60.1	371.0
29	62.5	448.0
30	65.7	523.0

NOTES. 1) Eutectic, 182°, 32 mole % KCl. 2) Transition point, 199°, 37 mole % KCl. 3) Transition point, 239°, 50 mole % KCl. 4) Transition point, 245°, 55 mole % KCl. 5) Above 245° and 55 mole %KCl, crystals of potassium chloride separated.

There was no indication of change of phase on the liquidus curve at the concentration between the eutectic at 193° and the transition point at 243°. However, there was a clearly fixed halt on the heating and cooling curves at 210°, corresponding to the compound, $HgCl_2 \cdot 2NH_4Cl$.

TABLE 4(Continued)

No.	Mole % NH_4Cl	Temp. of appearance of the first crystals
35	47.0	214.0
36	48.5	217.5
37	50.0	218.0
38	52.0	215.0
39	54.0	214.0
40	55.0	213.0
41	57.0	210.0
42	59.0	203.0
43	60.0	201.5
44	62.5	209.0
45	63.5	220.0
46	65.0	230.0
47	66.0	237.5
48	66.5	238.5
49	67.0	242.0
50	68.0	251.0
51	69.0	262.0
52	70.0	273.5
53	71.0	296.0
54	73.0	316.0

NOTES. 1) Transition points: 243° and 18.5 mole % NH_4Cl; 235° and 23.5 mole % NH_4Cl; and 214° and 33.5 mole % NH_4Cl. 2) Eutectic points: 198° and 38.7 mole % NH_4Cl, and 193° and 61 mole % NH_4Cl. 3) Maximum at 50 mole % NH_4Cl and 218°. 4) Transition point, 243° and 66.6 mole % NH_4Cl.

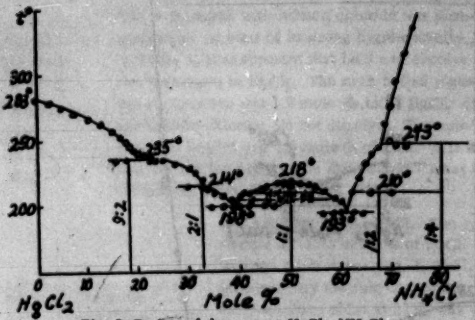

Fig. 2. Fusion of the system $HgCl_2$–NH_4Cl.

Above 243°, NH_4Cl crystallized from the melt. The liquidus curve was stopped at 316° by the distillation of the undissolved NH_4Cl.

TABLE 5

	No. of molecules found in the compound		
	$HgCl_2$	MeCl	H_2O
NH_4Cl [14]	2	1	1
	1	1	1
	2	3	1
	9	2	–
KCl • . . .	1	1	–
	1	2	1
NaCl•	1	1	–

DISCUSSION OF THE RESULTS

It is apparent from Figs. 1 and 2 and Tables 1-4 that the tendency for complex formation increases with the increase in the radius of the alkali metal cation. For example: in the LiCl–$HgCl_2$ system there was no chemical combination; in the system NaCl–$HgCl_2$, 2 compounds were formed; in the system KCl–$HgCl_2$, 4 compounds were formed; and in the system NH_4Cl–$HgCl_2$, 5 compounds were formed. The most pronounced type of compound was the compound (1:1), whose stability increased with the increase in the radius of the alkali metal cation. In the system NH_4Cl–$HgCl_2$ there is a maximum on the crystallization curve at 218° for this compound.

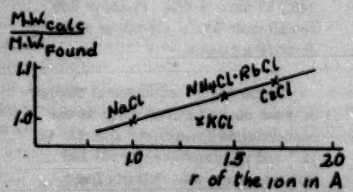

Fig. 3. The ratio $M_{calcd.}/M_{found}$ found as a function of the radius of the cation ($M_{calcd.}$ is the calculated molecular weight, M_{found} is the molecular weight obtained by cryoscopic methods).

The increased complex formation, in the order Li, Na, K, and NH_4 was accompanied by an increase in the angle of incidence on the crystallization curve of mercuric chloride. For cations of large radius, specifically for rubidium and cesium, a large increase in the tendency for complex formation, and a large increase in the angle of incidence of the crystallization curve of $HgCl_2$ must be expected.

The conclusion that complex formation increases with an increase in the radius of the alkali metal agrees well with the results of Beckman [6], if a graph is made of the deviation of the molecular weight found cryoscopically, from that calculated (Fig. 3). From the results

• Systems with NaCl and KCl were studied in the authors' laboratory.

in Fig. 3, it is seen, that this tendency increases in the order Na, K, NH_4, Rb, and Cs.

Lithium chloride behaved analogously to the alkaline earth metals in combination with $HgCl_2$ [8]. This property of lithium had previously been reported by A. G. Bergman.

The study of the ternary water-salts system $HgCl_2$–MeCl–H_2O, where MeCl=NaCl, KCl, and NH_4Cl, showed the same increasing tendency for complex formation. This can be readily seen from Table 5.

SUMMARY

1. The systems: $HgCl_2$–LiCl, $HgCl_2$–NaCl, $HgCl_2$–KCl, and $HgCl_2$–NH_4Cl were studied by the fusion method.

2. An increased tendency for complex formation in the melts, in the order Li → Na → K → NH_4 was found and was found to be accompanied by an increase in the angle of incidence of the same order, on the crystallization curve of $HgCl_2$.

3. The type of fusion diagram for the system $HgCl_2$–LiCl placed it in the same category as the systems "alkali earth chlorides—mercuric chloride".

4. A relation between the molecular weights obtained by cryoscopy and by calculation and the radius of the alkali metal ion, was found in Beckman's results.

5. Three polymorphic transformations in a narrow temperature range (203-213°) were found for the compound (1:1) in the system NH_4Cl–$HgCl_2$.

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PHYSICO-CHEMICAL ANALYSIS OF SYSTEMS OF MERCURIC HALIDES AND HALIDES OF AMMONIA AND THE ALKALI METALS

II. FUSION OF BROMIDE AND IODIDE SYSTEMS

I. N. Belyaev and K. E. Mironov

The results of the fusion studies on chloride systems are given in the previous communication. In this paper, the results of fusion studies on the systems: $HgBr_2$–NaBr, $HgBr_2$–KBr, $HgBr_2$–NH_4Br, HgI_2–NaI, HgI_2–KI, and HgI_2–NH_4I are given.

EXPERIMENTAL

Reactants: $HgBr_2$ — synthesized according to Reinders; HgI_2 — according to Karyakin [1]; sodium, potassium, and ammonium bromides and iodides were twice recrystallized commercial C.P. preparations.

Precedure: All of the iodide systems and that of $HgBr_2$–NaBr were studied by the visual-polythermic method, by reporting the appearance and disappearance of the first crystals, and by visually recording complete heating and cooling curves. For the systems $HgBr_2$–KBr and $HgBr_2$–NH_4Br, the liquidus curve was obtained visually by the appearance of the first and the disappearance of the last crystals. Below the liquidus curve, these sytems were studied by means of heating and cooling curves obtained by a recording potentiometer, IM-148 (the record was made by a plain thermocouple and a recording thermograph) and by recording thermograph (the record was made by a differential thermocouple). These experiments were conducted in closed vessels. The thermocouples, plain and differential, were of nichromeconstatan wire, 0.2 mm in diameter, and were calibrated by the melting points of naphthalene, cadmium, tin, and zinc. All transformations in the system were accurately registered by the plain and differential thermocouples.

I. Bromide Systems

System $HgBr_2$–NaBr. The experimental results are given in Tables 1-3 and Figs. 1-2.

As seen from Fig. 1, the curve, at the beginning of the crystallization, resembled the one reported in the first paper for the chloride system. The system was studied up to 26 mole % of NaBr. The crystallization curve had three main points, one of which was a eutectic point at 232° and 3.5% NaBr*, and two transition points at 243° and 15% NaBr and at 288° and 21% NaBr which corresponded to the compounds of the following probable composition: $HgBr_2 \cdot NaBr$ and $HgBr_2 \cdot 2NaBr$. NaBr crystallized above 288°. The melt boiled at 327° and the NaBr did not dissolve.

System $HgBr_2$–KBr. The system was studied up to 70% KBr. It had five main points; one of which, at 168° and 42.5% KBr, was the eutectic; two at 185° and 190° and 33.3% and 50% KBr were transition eutectic points, and two transition points at 218° and 207° and 17% and 55% KBr.

The transition eutectic points at 185° and 190° corresponded to: first, the melting point of the eutectic mixture of the compounds $KBr \cdot 2HgBr_2$ and $KBr \cdot 7HgBr_2$, and the melting point of the compound $KBr \cdot 2HgBr_2$; second, the melting point of the eutectic mixture of the compounds $KBr \cdot HgBr_2$ and $2KBr \cdot HgBr_2$ and the melting point of the compound $KBr \cdot HgBr_2$. The transition points at 218° and 207° appeared to be the incongruous melting points corresponding to the compounds $KBr \cdot 7HgBr_2$ and $2KBr \cdot HgBr_2$. The results, therefore, showed that four compounds: $KBr \cdot 7HgBr_2$, melting incongruously at 218° and 17% KBr; $KBr \cdot 2HgBr_2$, melting point 185°; $KBr \cdot HgBr_2$, melting point 190°, and $2KBr \cdot HgBr_2$ melting incongruously at 207° and 55% KBr.

The melts from 35-52% KBr were viscous (glycerine like) and were very prone to supercooling. The experimental results for this part of the liquidus curve were obtained at the disappearance of the last crystals, as well as the appearance of the first; transition temperatures below the liquidus curve were obtained by the heating curve because at this concentration, the transition points were registered at much lower temperatures

* All percentages are molecular.

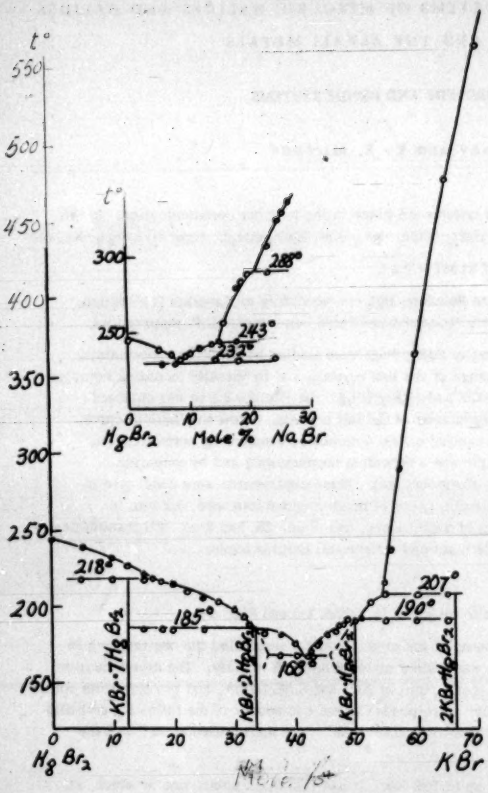

Fig. 1. The fusion of the system $HgBr_2$–NaBr and $HgBr_2$–KBr.

TABLE 1

Fusion of the system $HgBr_2$–NaBr.

Mole % NaBr	Temperature of appearance of first crystals
0.0	243.0
5.0	239.0
7.0	236.0
8.5	232.5
9.5	235.0
10.0	238.0
12.0	239.0
14.0	242.5
15.0	243.5
16.0	256.5
18.0	277.5
18.8	281.5
20.0	286.0
23.5	306.0
25.0	321.0
25.8	325.5
30.0	Boiled at 327°, NaBr did not dissolve

(20-30°) on the cooling curve because of supercooling.

System $HgBr_2$–NH_4Br. The system was studied up to 75 mole % of NH_4Br. When the concentration of NH_4Br was larger, it distilled and the melt boiled at 380°.

The results of thermal analysis showed that four compounds, melting with decomposition, were formed: $2NH_4Br \cdot 9HgBr_2$, $2NH_4Br \cdot 3HgBr_2$, $2NH_4Br \cdot HgBr_2$, and $4NH_4Br \cdot HgBr_2$; which had the following transition points (respectively): 122° and 24% NH_4Br, 155° and 40.5% NH_4Br, 201° and 60.5% NH_4Br, and 266° and 67% NH_4Br. A transformation was found on the cooling curve at 5-17.5% NH_4Br and 182-202° which corresponded to the solid state of the compound of composition $NH_4Br \cdot 7HgBr_2$. The compounds $2NH_4Br \cdot 3HgBr_2$ and $2NH_4Br \cdot HgBr_2$ formed a eutectic at 140° and 47.5% NH_4Br.

In contrast to the previous systems, the compound of composition 1:1 was absent from the system NH_4Br–$HgBr_2$. The melt at concentrations of 35-60% NH_4Br, was characterized by a high viscosity and a great tendency to supercool.

II. Iodide Systems

The experimental results for the iodide systems are given in Tables 4-5 and Figs. 3-4.

System HgI_2–NaI. The system, according to the type of its crystallization curve, resembled the previous sodium chloride and bromide systems. A transition point, corresponding to an incongruously melting chemical

TABLE 2

Fusion of the system $HgBr_2$–KBr

Mole % KBr	Temperature of the appearance of the first crystals	Transition points below the liquidus line
0.0	244.0	–
5.0	238.5	218
10.0	232.0	218
12.5	227.0	–
15.0	222.0	218
16.5	219.0	–
18.0	217.0	185
20.0	215.0	185
22.5	210.0	–
25.0	206.0	185
27.5	203.0	–
30.0	199.0	–
31.5	193.0	–
35.0	183.0	–
37.5	182.0	168
40.0	176.0	168
41.8	168.0	–
42.0	271.0	168
43.5	175.0	–
43.7	176.0	–
45.0	182.0	–
45.4	182.0	–
46.5	184.0	–
47.1	187.0	–
48.0	188.0	–
48.5	191.0	–
50.0	190.0	–
51.0	192.0	–
52.5	201.0	–
54.0	206.5	–
55.0	214.0	207, 190
56.0	235.0	–
57.5	288.0	–
60.0	362.0	207, 190
65.0	476.0	207, 190
70.0	561.0	–

compound, was observed on the crystallization curve; its presence agreed with the results of Delimarsky and Kolloti [2], on the decomposition potential in melts. There was a eutectic point at 216° and 26% NaI. When 0-11% of NaI was added to the mercuric iodide, the transition temperature of the change of the yellow modification of HgI_2 to the red fell, which showed the presence of chemical compounds with HgI_2 in this region of the solid solution.

Above 256°, NaI crystallized from the melt. Further study was prevented by the violent boiling of the melt at 392° and 46.5% NaI.

TABLE 3

Fusion of the system $HgBr_2$–NH_4Br

Mole % NH_4Br	Temperature of the appearance of the first crystals	Transition points below the liquidus line
0.0	243.0	–
4.1	239.5	–
5.0	238.0	222, 182
8.4	237.0	–
10.0	235.0	222, 198
15.0	232.0	222, 202
17.5	227.0	222, 200
18.1	226.0	–
20.0	225.0	222, 155
22.5	221.5	155
23.4	221.5	–
25.0	221.0	155
27.5	220.0	–
30.0	216.0	155
31.3	212.0	–
32.5	208.0	155
33.4	205.5	–
34.6	200.5	–
35.0	199.0	155
37.5	189.0	155
39.0	170.0	–
40.0	159.0	155
42.5		140
43.2	153.5	–
45.0	151.0	140
46.2	148.0	–
47.5	140	140
47.9	146.0	–
49.9	165.0	–
50.0	166.0	140
52.0	177.5	–
53.6	184.0	–
55.0	189.0	140
55.2	190.5	–
57.3	194.0	–
57.5	–	140
59.2	199.0	–
60.0	200.0	–
61.0	208.0	–
62.7	227.0	201
64.1	238.0	–
65.0	248.0	201
67.5	–	201, 266
70.0	316.5	201, 267
75.0	371.0	268

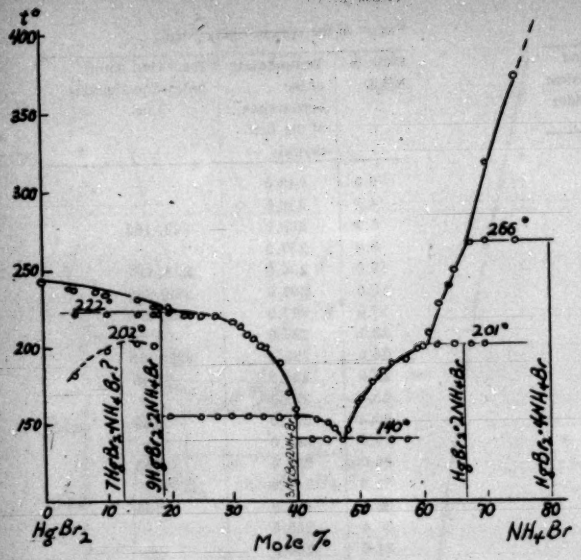

Fig. 2. Fusion of the system $HgBr_2$–NH_4Br

TABLE 4

Fusion of the System HgI_2–NaI

Mole % NaI	Temp. of the appearance of the first crystals	Transition points below the liquidus line	Mole % NaI	Temp. of the appearance of the first crystals	Transition points below the liquidus line
0.0	257.5	127	23.8	226	–
3.9	255.0	–	25.0	220.5	120, 216
4.8	254.0	125	26.6	228.0	–
7.5	253.0	–	28.2	238.5	–
8.3	252.0	120, 217	29.7	253.0	120, 216
10.8	249.0	–	31.2	269.5	–
12.0	248.0	121, 216	33.6	294.0	216, 256
13.9	246.0	–	35.7	317.0	–
15.0	242.0	–	37.7	338.0	–
16.0	241.0	–	39.6	349.0	–
18.2	239.0	120, 216	41.4	367.0	–
20.2	237.0	120, 216	43.0	378.0	–
22.0	232.0	–	44.7	390.0	216, 256
23.2	228.0	–	46.2	At 372°, the melt boils	

System HgI_2–KI. The fusion and the electroconductivity of the system was previously studied by one of the authors. The results of the fusion studies are given in Fig. 3.

System HgI_2–NH_4I. The system was studied up to 75% NH_4I (Fig. 3, Table 5). The presence of two chemical compounds of composition $HgI_2 \cdot 2NH_4I$, and $HgI_2 \cdot 4NH_4I$ was shown on the liquidus curve. On the crystallization curve there was a transformation point at 120°, corresponding to the change of HgI_2 from the yellow to the red modification. The presence of solid solutions of HgI_2 with the compound $2NH_4I \cdot HgI_2$ at 0-7% NH_4I was shown on the cooling curve.

When heated over 210°, violet fumes of iodine vapors filled the test tube; because of this, the liquidus curve after 57% NH_4I was only approximate. At 388° the melt boiled, depositing iodine crystals as it distilled upwards.

Discussion of the results

As seen from the Figures and Tables, the complex formation of the systems $HgBr_2$–MeBr and HgI_2–MeI, as well as that of the systems $MgCl_2$–MeCl, increases with the increase of the volume of the alkali metal cation. The systems $MnCl_2$–MeCl, MgF_2–MeF, and others [3,4] behave analogously.

In the series $HgHal_2$, with the increase of the halogen volume (Cl = 1.81 A, Br = 1.96 A, and I = 2.20 A) the tendency for complex formation decreases, which is shown by the number of

TABLE 5

Fusion of the system HgI_2–NH_4I.

Mole % NH_4I	Temp. of appearance of the first crystals	Transition points below the liquidus line
0.0	257.5	127
5.0	254.0	121
7.7	250.0	–
10.0	248.0	120
10.3	248.0	–
12.0	246.0	–
13.2	242.5	–
13.7	242.0	–
14.3	240.0	–
15.0	237.5	–
15.1	238.0	–
15.4	236.0	–
16.6	235.0	–
17.6	232.0	–
18.0	232.5	–
18.7	231.0	–
19.4	230.0	–
19.6	228.5	–
20.7	227.0	120
22.6	219.0	–
24.4	215.0	113,120
25.6	210.0	–
27.5	205.0	–
29.5	197.0	–
31.0	193.0	113,120
33.8	180.0	–
35.0	160.0	113, 120
37.5	145.5	–
38.5	140.0	–
39.4	136.0	–
40.1	132.0	113, 120
40.8	126.0	–
41.5	123.0	–
42.2	122.0	–
42.9	119.0	–
43.1	116.0	–
43.9	126.0	–
44.9	139.0	113
46.2	150.5	–
47.3	160.0	–
48.4	169.0	–
49.5	176.5	–
50.0	182.0	113
50.0	182.0	–
52.3	194.5	–
54.2	201.5	–
56.1	207.0	–
58.0	210.5	–

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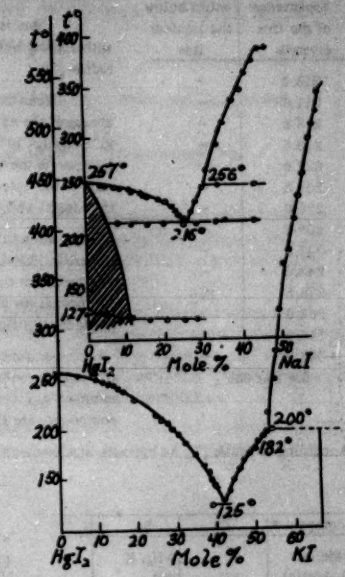

Fig. 3. Fusion of the systems HgI_2–NaI and HgI_2–KI.

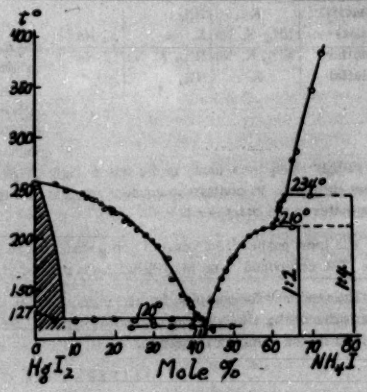

Fig. 4. Fusion of the system HgI_2–NH_4I.

TABLE 5 (Continued)

Mole % NaI	Temp. of appearance of the first crystals	Transition points below the liquidus line
59.6	211.0	–
60.0	211.0	–
60.3	216.0	–
61.0	219.5	–
61.8	227.0	–
62.1	231.5	–
62.5	236.0	–
62.9	239.0	–
63.2	242.5	–
63.3	243.0	–
65.0	278.5	210
66.2	288.0	–
70.1	344.0	234
72.5	385.0	–
74.8	Boils at 388°	

compounds formed. Therefore, in the molten state, in contrast to the aqueous solutions [5], the tendency for complex formation by alkali metal halides with mercuric halides increases in the order I–Cl–Br.

There is a smaller difference in the tendency for complex formation with $HgHal_2$ when the anionic volume is increased along with the cationic radius [6].

When the volume of the halides increases and the cation is unchanged, the eutectic melting point of the melt is lowered (for example: KCl–$HgCl_2$ = 185°, KBr–$HgBr_2$ = 171°, and KI–HgI_2 = 125°). With an increase in the volume of the cation in the systems $HgHal_2$–MeHal, a shift of the eutectic melting point of the melt occurs towards that of the MeHal which results in a decrease.

When all of the results are compared, it is seen that the compounds richest in $HgHal_2$ are the chlorides and those rich in MeHal the iodides. The bromides occupy an intermediate position. The most characteristic compounds for all of the halides are $2MeHal \cdot HgHal_2$ and $MeHal \cdot HgHal_2$ (besides $NH_4I \cdot HgI_2$).

For a more descriptive presentation of the relation of the type of compounds to the volumes of the halides and the metal, see Table 6. A summary is given, where the cations, which give the resulting type of compound, are listed under the heading of the halogen.

According to Wells [7], an opposite arrangement must be used for aqueous solutions.

TABLE 6

Type of compound	Cl	Br	I
$7HgHal_2 \cdot MeHal$		NH_4, K	
$4.5HgHal_2 \cdot MeHal$	NH_4	NH_4	
$3HgHal_2 \cdot MeHal$	NH_4	NH_4	
$2HgHal_2 \cdot MeHal$	NH_4	K	
$3HgHal_2 \cdot 2MeHal$	K	NH_4	
$HgHal_2 \cdot MeHal$	NH_4, K, Na	K, Na	K, Na ?
$HgHal_2 \cdot 2MeHal$	NH_4, K, Na	NH_4, K, Na	K, Na
$HgHal_2 \cdot 4MeHal$	K	NH_4	NH_4

SUMMARY

1. The systems $HgBr_2$–NaBr, HgI_2–NaI, HgI_2–KI, and HgI_2–NH_4I were studied by means of the visual-polythermic method. The systems $HgBr_2$–KBr and $HgBr_2$–NH_4Br were studied by means of the visual-polythermic and by thermal methods, with recording of the heating and cooling curves.

2. The tendency for complex formation between the mercuric halides and alkali metal and ammonium halides in melts was shown. Two compounds whose composition was not determined, were formed in the system $HgBr_2$–NaBr: four compounds, $KBr \cdot 7HgBr_2$, $KBr \cdot 2HgBr_2$, $KBr \cdot HgBr_2$, and $2KBr \cdot HgBr_2$ were formed in the system $HgBr_2$–KBr; five compounds, $NH_4Br \cdot 7HgBr_2$, $2NH_4Br \cdot 9HgBr_2$, $2NH_4Br \cdot 3HgBr_2$, $2NH_4Br \cdot HgBr_2$ and $4NH_4Br \cdot HgBr_2$ were found in the system HgBr–NH_4Br; one compound, of clear composition, NaI–HgI_2 was formed in the system HgI_2–NaI. In contrast to aqueous solutions the tendency for complex formation and the stability of the complex increases in the order I – Br – Cl.

3. The most pronounced forms of compounds rich in $HgHal_2$ were the chlorides and rich in MeHal the iodides. The compound type $Me_2[HgHal_4]$ was present in all systems.

4. The tendency for complex formation increases in the chloride and bromide systems with an increase in the ionic radius of the alkali metal. In iodide systems, the increase in the ionic radius of the alkali metal has little effect on the complex formation.

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KINETICS AND MECHANISM OF THE REACTION OF ACTIVE CHLORINE WITH ORGANIC COMPOUNDS

VIII. OXIDATION OF FORMIC ACID IN ALMOST NEUTRAL AND BASIC SOLUTIONS

E. A. Shilov, A. I. Slyadnev, and G. V. Kupinskaya

The oxidation of formic acid in acid solutions occurs by means of the action of molecular chlorine on the formate ion [1]. The authors show herein that in basic solutions the oxides of chlorine act as the oxidizing agent, with the hydroxyl ion having an activating effect. At the same time, certain secondary effects become apparent during the oxidation reaction.

Composition of the reaction mixture. As the pH of the solution increases, the form of the active chlorine changes according to the equation $Cl_2 \longrightarrow HOCl \rightarrow OCl^-$. The amount of each of the components can be calculated from the electrolytic dissociation constant, K_ϑ, of hypochlorous acid and the hydrolysis constant, K, of chlorine. When the concentration of the chloride ion is small, each mixture remains practically two-component because Cl_2 and OCl cannot exist together in commensurate concentrations.

Let h be the concentration of the hydrgen ion, c that of the chloride ion, and C the combined concentration of active chlorine. It is easy to show that for mixtures of HOCl and OCl^- the following expressions hold:

$$[HOCl] = \frac{h \cdot C}{h + K_\vartheta} \quad \text{and} \quad [OCl^-] = \frac{K_\vartheta C}{h + K_\vartheta};$$

For mixtures of Cl_2 and HOCl the expressions are:

$$[HOCl] = \frac{K \cdot C}{hc + K} \quad \text{and} \quad [Cl_2] = \frac{hcC}{hc + K}.$$

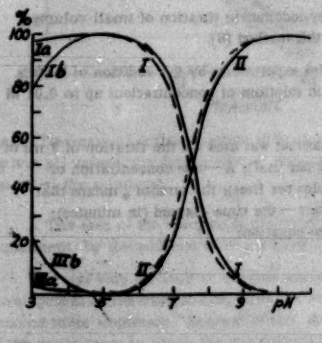


Fig. 1. Composition of chlorine solution vs. the pH.
I) % HOCl; II) % OCl, the solid line is for $K_\vartheta = 3.1 \cdot 10^{-8}$, the broken line for $K_\vartheta = 4.1 \cdot 10^{-8}$; Ia) % HOCl in the presence of 0.01 molar chloride ion; Ib) % HOCl in the presence of 0.1 molar chloride ion; IIIa) % Cl_2 in the presence of 0.01 molar chloride ion; IIIb) % Cl_2 in the presence of 0.1 molar chloride ion.

The given formulas show that when the pH is constant, the concentration of HOCl and OCl^- are proportional to the usual concentration of the active chlorine, C.

The values of the constant K_ϑ were obtained by several methods (see the summary [2] and [3]) and vary widely. The values obtained by the electrometric titration of hypochlorous acid are the more reliable.

During these studies, the value of the constant K_ϑ was determined by the titration of the HOCl solutions with a glass electrode in the presence and absence of salt. The value for $K_\vartheta = 3.3 \cdot 10^{-8}$ at 20° was obtained for salt concentrations of about 0.013; here the thermodynamic constant was equal to $3.08 \cdot 10^{-8}$ which is very close to the more reliable values obtained by the same method (average $3.0 \cdot 10^{-8}$). In the presence of 0.5 M KNO_3, the constant K_ϑ increases to $4.1 \cdot 10^{-8}$.

The value of the hydrolysis constant, K, for the chloride ion is of secondary importance. The result of Yakovkin, equal to $3.78 \cdot 10^{-8}$ at 20° was satisfactory.

The curves in Figure 1 were constructed with aid of the values of K_ϑ and K which show the changes in percentage composition of solutions of active chlorine at pH's of 3 to 11. The composition curve, calculated for the thermodynamic value of the constant

K_0 ($3.1 \cdot 10^{-6}$) is represented by the solid line, that for the salt, constant K_s ($4.1 \cdot 10^{-6}$) by the broken line. In acidic solutions, the determination was made at two values of the chloride ion concentration — 0.01 molar and 0.1 molar.

Knowledge of the concentration of chlorine oxide, which forms according to the equilibrium reaction $2HOCl \rightleftarrows Cl_2O + H_2O$, would be valuable for the discussion of the results. According to Goldschmidt [4], at 0°

$$K' = \frac{[Cl_2O]}{[HOCl]^2} = 0.00096.$$

Roth [5] recalculated the results of Goldschmidt and obtained the value $K' = 0.00355$ (0°). There are no determinations for K' at other temperatures, but Roth found for 19° the value $K' = 0.0089$ by an indirect method. In all cases, in dilute solution, the concentration of Cl_2O is very small when compared to the concentration of hypochlorous acid.

Experimental Method

Preparations. Pure sodium formate was twice recrystallized from water. For comparison, the salt was made from pure formic acid and sodium hydroxide. The salt preparations were dried at 110-120° and carefully tested for the presence of oxalate, carbonate, and chloride impurities. The analytically determined composition of sodium did not differ from the calculated by more than 0.1%.

Hypochlorous acid was obtained by vacuum distillation of solutions obtained by treating chlorine water with silver phosphate. The amount of chlorine in the HOCl solutions was controlled by electrolysis [6].

The buffer solutions were prepared from recrystallized phosphate salts and bases; they were tested in control experiments for their ability to reduce active chlorine.

An electrometric instrument, built according to Sokolov and Pchelin [7], was used to measure the pH in the first series of experiments by means of a glass electrode. In the main series of experiments, an apparatus of the Cambridge system with direct calculation of the pH values was used. The apparatus was standarized with standard solutions of borax and potassium acid phthalate.

The reaction solutions were placed in the thermostat, mainly at 20° ± 0.02°. Several experiments were made at 0°. The flask was covered with metal foil to protect it from light. The test tubes, about 2 ml, were filled by pneumatically regulated pipets, in one series by weight, and in another by volume. The specific gravity of the solution was determined in a parallel experiment in a pycnometer. In view of the relative nonvolatility of hypochlorous acid from solutions, the precautions so necessary for working with chlorine water [1] were not needed.

The amount of active chlorine in the test tube was determined by iodometric titration of small volumes by means of a pneumatic apparatus, observing the usual precautions for this method [8].

The decomposition of hypochlorous acid was controlled in parallel experiments by the addition of buffers. In agreement with Foerster [9], the decomposition of hypochlorous acid in solutions of concentrations up to 0.01 M amounted to less than 1% in 1 hour.

Designation of the symbols. a — the volume of 0.01 N thiosulfate that was used for the titration of 1 ml of the reaction mixture; C — the concentration of active chlorine (in moles per liter); A — the concentration of formate (in moles per liter); Φ — the concentration of phosphate (in moles per liter); the symbol $_0$ means that the given value of the concentration was the initial value of the reaction; t — the time elapsed (in minutes); q' — a third order constant calculated from the constant value of A by the equation:

$$q' = \frac{1}{t} \cdot \frac{1}{AC_0} \cdot \frac{a_0 - a}{a}$$

Experimental Procedure

Concentrations of 0.005-0.01 M for the hypochlorous acid and 0.25-0.5 M for the formate were taken for the kinetic measurements. At higher concentrations, the HOCl tended to decompose in side reactions, and at lower concentrations of formate than those given, the reaction was so slow that the amount of decomposition of the active chlorine increased during the normal course of the reaction.

During the kinetic experiments on the oxidation of formate, an unsatisfactory reproduction of the experimental results was found. Experiments run at various times showed disagreements which could not be accounted

for by the possible experimental error. As an explanation for these results, it was found that the reaction mixture was somewhat sensitive to small amounts of ammonia; this circumstance suggested the known case of the activity of hypochlorous acid for the oxidation of cellulose [10].

Metallic impurities such as copper and ferric salts did not show any catalytic activity.

Because comparatively large amounts of formate and phosphate were used in the experiments, the possibility that small amounts of highly oxidizable impurities were present in them had to be considered.

However, in spite of all of possible measures taken to exclude the possible deterrents (in particular the action of light), the spread of the experimental results was much greater than in other studies on kinetics of reactions with active chlorine. Because of this, when the results of the kinetics of the oxidation of formic acid with active chlorine at a pH of 5 to 10 were examined, certain fixed and sharply defined limits had to be used.

Fig. 2 shows the results of several experiments with identical initial concentrations of reagents: $A_0 - 0.25$ molar, C_0 — about 0.005 molar. The temperature was 20°. It can be seen that at pH values of 5.5-7, the rate of the reaction depended little on the pH; at higher pH values, the reaction slowed down and finally stopped.

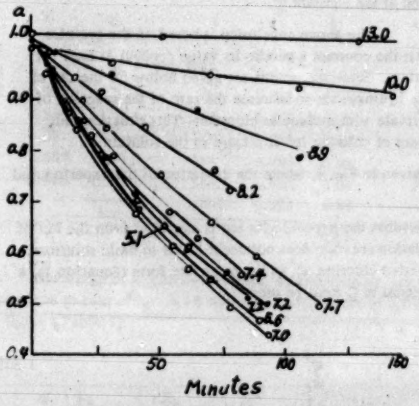


Fig. 2. Decrease of active chlorine titer in reaction mixtures at various pH values (the figures next to the curves correspond to the pH of the solutions).

The conclusions from the kinetic equation

The calculation of the experimental results from each determination, at not too high values of the pH, was obtained at the first stage of the reaction by the secondary kinetic equation for the function of the concentration of the active chlorine:

$$-\frac{dC}{dt} = q'AC^2. \qquad (1)$$

At about half decomposition, the second order constants for the function of C were found to have a tendency to grow. This increase was mainly tied up with the formation of chloride ions. In fact, if potassium chloride is previously introduced into the mixture, the reaction rate increases, more or less, as a function of the concentration of the chloride ion (Fig. 3).

The rate of the reaction is also increased when the new reaction is run in the solution from the old experiment, by the addition of new aliquot of hypochlorous acid to the mixture.

It was very difficult to account accurately for the effect of the chloride ion, and especially on the development of the experiment, when the small losses of hypochlorous acids from decomposition and evaporation become more important. Because of this, examination of the results of the experiments was limited to that part of the experiment in which the concentration of the chloride-ion was still low enough to have no influence on the value of the rate constant. The results of several typical experiments are given below (at 20°). The pH during the course of the reaction was kept with the limits of 0.01-0.02 pH units.

Upon comparing the results of various experiments, it was shown that the constant q' remains stable within experimental limits, with constant pH values, while A_0 changes from 0.05 to 0.5 m and C_0 from 0.0025 to 0.02 m.

With the aid of the constant q', the importance of the reaction by means of elementary chlorine, which is, as is known, the main active agent in acidic solutions [1], can be evaluated. By considering this reaction to be parallel to the reaction by means of hypochlorous acid, it can be shown:

$$-\frac{dC}{dt} = \underset{I}{q'AC^2} + \underset{II}{kA\,[Cl_2]}.$$

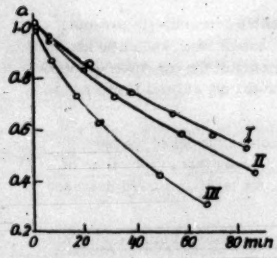


Fig. 3. Velocity of Reaction as a function of chloride concentration
I) without any additions, II) 0.01 molar KCl, III) 0.1 molar KCl. For all experiments: $A = 0.25$, $C = 0.005$, $\Phi = 0.2$, pH = 7.55

The value of k in acidic solutions is about 300, the value of q' in the experiments in this study of low pH values approaches 8. Considering that, at low pH values, the main part of the active chlorine is in the form of HOCl, and with the aid of the hydrolysis constant for chlorine, the following ratio of the reaction path II to I for the total reaction path was calculated:

at pH = 5	5.5	6	7	8	9
ratio $\frac{II}{I}$ = 0.2	0.06	0.02	2.10^{-3}	2.10^{-4}	2.10^{-5}

Therefore, at low pH values only, does the reaction by means of Cl_2 have a noticeable effect on the value of the constant q'. Starting at pH 6, this reaction path does not have to be taken into account for calculation of the constant q'.

The above conclusion is based on the premise that the constant k retains its value ($\approx$300) at high pH values. However, results are given below for the use of the hydroxyl ion to increase the rate of the reaction of formate with molecular chlorine. This situation can have a noticeable effect, in cases where a certain amount of chloride ion is present in the solution.

The dependence of the constant q' on the pH is given in Fig. 4, where the deviation of the experimental results from the average is shown.

By evaluating the curve shown in Fig. 4, it is seen that the hypochlorite ion is excluded from the list of direct oxidizing agents for the formate because the oxidation reaction does not occur at all in basic solutions. Because of the appearance of the concentration of the active chlorine, C, in the quadratic form (Equation 1), a concentration for the hypochlorous acid directly proportional to C must be used:

$$[HOCl] = \frac{h\,C}{h + K_0},$$

where $h = [H^+]$.

The kinetic equation now takes the form:

$$-\frac{dC}{dt} = k'' \frac{h^2}{(h + K_0)^2} AC^2 \quad (2)$$

From equations (1) and (2)

$$k'' = q'\left(\frac{K_0}{h} + 1\right)^2.$$

Table 1 contains the results of the calculations for the values of k'' by means of this formula, using the value of q' obtained from curve in Figure 4. The salt solution value for K_0, $4 \cdot 10^{-8}$, was taken.

Unexpectedly, k'' does not remain constant but increases with increasing pH. It is not difficult to show that the increase of k'' is not related directly to the concentration of either the hydroxyl ion or the hypochlorite ion.

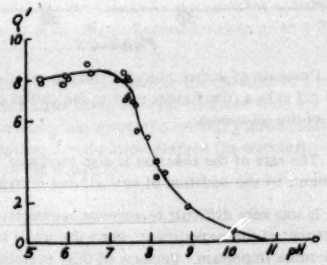


Fig. 4. The variation of the constant q' with the pH.

Experiment 16
pH 5.38, $A_0 = 0.25$
$C_0 = 0.005$, $\Phi = 0.2$

t	a	q'
0	1.015	–
6	0.956	8.1
17.7	0.865	7.7
25.6	0.812	7.7
38.8	0.731	8.0
47.5	0.683	8.0
63.8	0.600	(8.4)
76	0.551	(8.7)
97	0.477	(9.2)
		8.0

Experiment 54
pH 7.16, $A_0 = 0.25$
$C_0 = 0.005$, $\Phi = 0.2$

t	a	q'
0	1.002	–
6.8	0.940	7.8
28.9	0.789	7.44
55.8	0.649	7.8
76.3	0.562	8.2
93.2	0.497	(8.7)
		7.8

Experiment 28
pH 7.5, $A_0 = 0.25$
$C_0 = 0.005$, $\Phi = 0.2$

t	a	q'
0	1.008	–
5.2	0.957	8.0
16.9	0.862	8.0
39	0.718	8.2
62	0.587	(9.1)
70	0.552	(9.3)
120	0.425	(9.0)
		8.1

Experiment 69
pH 7.74, $A_0 = 0.25$
$C_0 = 0.005$, $\Phi = 0.4$

t	a	q'
0	1.013	–
7.2	0.956	6.6
19.5	0.895	5.4
29.8	0.845	5.28
50	0.751	5.4
71	0.661	5.8
88	0.591	(6.4)
114	0.495	(7.3)
		5.6

Experiment 18
pH 8.9, $A_0 = 0.25$
$C_0 = 0.005$, $(KHCO_3) = 0.2$

t	a	q'
0	1.013	–
7.8	0.994	1.9
30.7	0.950	1.7
64	0.880	1.9
105	0.79	2.1
159	0.687	(2.3)
211	0.613	(2.4)
		1.9

Experiment 21
pH 9.95, $A_0 = 0.25$
$C_0 = 0.005$, $(K_2CO_3) = 0.2$

t	a	q'
0	1.008	–
37	0.972	(0.79)
69	0.951	0.68
105	0.929	0.64
144	0.915	0.56
182	0.890	0.58
255	0.853	0.56
309	0.822	0.58
		0.60

However, the results of the experiments may be expressed by means of two kinetic equations, one of which is proportional to the concentration of the OH^-.

$$-\frac{dC}{dt} = k_2 A[HOCl]^2 + k_2 A[HOCl]^2[OH^-] \quad (3)$$

or

$$-\frac{dC}{dt} = (k_2 + k_2' \cdot [OH^-])A[HOCl]^2.$$

Evidently,

$$k_2 + k_2' [OH^-] = q' \left(\frac{K_0}{h} + 1\right)^2 = k^*. \quad (4)$$

The value of k_2 can be obtained, by considering that at pH 5-6, the value of $k'[OH^-]$ is still very small in comparison to that of k_2: $k_2 = 8$ was used. The values of $k_2'[OH^-]$ and k_2' were found from Formula (4) by using this figure (Table 1).

TABLE 1

pH	q'	$\frac{K_0}{h} + 1$	$\left(\frac{K_0}{h} + 1\right)^2$	k^*	$k_2'[OH^-]$	$10^{-8} k_2'$
5.5	8	1.013	1.04	8.3	0.3	0.95
6	8.2	1.04	1.08	8.9	0.9	0.90
7	8.4	1.4	1.96	16.5	8.5	0.85
8	5	5	25	125	117	1.17
9	1.6	41	1681	$2.7 \cdot 10^3$	$2.7 \cdot 10^3$	2.7
10	0.4	401	$1.6 \cdot 10^5$	$6.1 \cdot 10^4$	$6.4 \cdot 10^4$	(6.4)
						$k_2' \simeq 1.10^8$

The conditions for the determination of k_2' are generally not very favorable for accuracy. At low pH values, k_2 must be calculated from the difference between $k^* - k_2$. At high pH values the value of k_2' becomes very inaccurate because it is necessary to multiply q' by the coefficient $\left(1 + \frac{K_0}{h}\right)^2$, which contains a large amount of errors in the values of K_0 and h.

A study of these results shows that the permanency of the constant k_2' at least in the order of its magnitude, confirms the presence of a kinetic term proportional to the concentration of the OH^-.

Effect of the buffers added. The salts of the weak acids in concentrations of 0.1-0.4 showed a small, and in most cases, a moderating effect upon the reaction. Phosphates were less active than borates and phthalates, and in basic media, could, apparently increase the reaction rate slightly. The data for this summary is found in Table 2, where the results of several experiments, under the best possible parallel conditions, are given. For non-buffered solutions where the pH gradually increased, the constants and the pH for zero decomposition were used.

TABLE 2

Experiment	pH	Buffer	Molar concentration of buffer salt	q'
19	5.39	–	–	8.8
17	5.4	Phthalate	0.1	6
16	5.38	Phosphate	0.2	8
31	7.4	–	–	6
32	7.4	Nitrate	0.2	6.8
38	7.4	Phosphate	0.2	7.8
30	7.4	Phosphate	0.4	8
47	8.2	–	–	2.0
45	8.2	Borate	0.2	1.1
46	8.2	Phosphate	0.2	3.2

Temperature coefficient for the reaction rate. Several kinetic experiments on the oxidation of formate at 0°, without the addition of buffers, were made. These experiments showed that a decrease in the temperature of 20° caused an almost ten-fold decrease in the reaction rate. Calculation of the constants q' and k_2' was difficult because the glass electrode could not be used to measure the pH at 0° and an accurate value of the electrolytic dissociation constant for hypochlorous acid for 0° was not known.

Mechanism of the Oxidation of the Formate ion.

The quadratic form, in which the concentration of HOCl is found in the Kinetic Equation (3), shows that the active oxidizing agent for the oxidation of formate appears to be chlorine oxide, which is related to the concentration of HOCl by the equilibrium equation:

$$2HOCl \rightleftharpoons Cl_2O + H_2O.$$

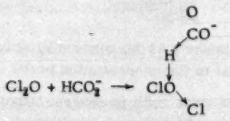
As is known, certain addition reactions of HOCl proceed by means of chlorine oxide, wherein the Cl_2O formation rate can limit the overall reaction rate [11]. The consecutiveness of these reactions is due to the fact that the concentration of the organic compound enters into the kinetic equation in a lower order. In these cases an increase in the hydroxyl ion concentration, which increases the rate of chlorine oxide formation, increases the reaction and removes, or lessens, the consecutive effect. The reactions studied go so slowly that the reaction for the formation of the chlorine oxide cannot limit the overall oxidation rate. Because of this, the equilibrium concentration of chlorine oxide is always assured in the experiments on the oxidation of formate. In agreement with this, no signs of consecutiveness were noticed upon increasing the formate concentration. Therefore, some other explanation for the catalytic action of the hydroxyl ion must be sought.

The form of the second term of the Kinetic Equation (3) leads to two possibilities: the OH^- acts, either on the hypochlorous acid, or on the formate ion. These possibilities are kinetically inseparable. In the first case, the product of $[HOCl]^2\,[OH^-]$ can be changed to the proportional quantity $[HOCl]\,[OCl]$, and in this way one returns to Kaufman's hypothesis postulating the existence of the complex $HOCl \cdot OCl^-$ [12], which is disclaimed by the author at the present time [10]. Kinetic considerations in other reactions of hypochlorous acid give no evidence for the existence of the Kaufman type complex compounds.

On the other hand, the action of the hydroxyl ion on the formate would indicate that the formate ion form a salt of orthoformic acid with the hydroxyl ion:

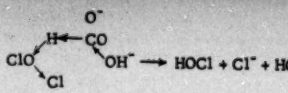
$$HCO_2^- + OH^- \rightleftharpoons \begin{bmatrix} OH \\ HCO \\ O \end{bmatrix}^{--}.$$

If such a reaction were allowed, the form of the Kinetic Equation (3) would be explained. However, it is difficult, apparently, to assign such a degree of acidity to the formate ion, which is necessary in order to lead to the formation of a sufficient amount of orthoformate salts to account for the observed reaction rates. Because of this, it is proposed that the hydroxyl ion acts, at the time of the reaction, on the complex which forms initially between the chlorine oxide and the formate ion according to the following outline:



(I)

The complex (I) supposedly can split into stable compounds without the aid of the hydroxyl ion, by eliminating CO_2 by the action of a molecule of water. However, decomposition of the complex proceeds more readily if the OH^- enters into the reaction:



Therefore, the increase in the reaction rate is due to the nucleophyllic effect of the hydroxyl ion.

An analogous proposal can be made to explain the catalytic action of the chloride, which was shown experimentally above. As was shown during the discussion of the amount of the reaction going by means of elementary chlorine, the reaction by means of Cl_2 becomes insignificant as compared to the reaction by means of HOCl even at pH values of 6-7. However, this conclusion was made on the basis of the comparison of reaction rates in acidic media when the action of OH^- is absent. If it is considered that the hydroxyl ion can ease the decomposition of the complex between chlorine and the formate ion, then the action of the chloride ion must also be more effective at higher pH values. This is, possibly, related to the increase of the reaction rate on the increase of the concentration of the chloride ion in the reaction mixture.

SUMMARY

1. The kinetics of the oxidation of formic acid at pH values of 5 to 10 with small concentrations of the chloride ion can be expressed by the general kinetic equation:

$$-\frac{dC}{dt} = k[HCO_3^-][Cl_2] + k_1[HCO_3^-][HOCl]^2 + k_2'[HCO_3^-][HOCl]^2[OH^-].$$

At 20° $k_1 = 8$, $k_2' \sim 1 \cdot 10^5$; k on the basis of previous measurements [1] is equal to ~ 300; in agreement with which, the first term in the kinetic equation has a definite value only when the pH is at the lowest value in the range studied.

2. The chlorine ion increases the reaction rate somewhat, which leads to the increase of the third order constant during the development of the reaction.

3. Salts of weak acids have a small moderating or stimulating effect on the oxidation reaction of formic acid.

4. At 0° the oxidation reaction of the formate is about 10 times slower than at 20°.

5. The main oxidizing agent for the formate in the pH range studied appears to be chlorine oxide. The catalytic action of the hydroxyl, expressed in the last term of the kinetic equation, is explained by the nucleophyllic effect of the hydroxyl ion, which aids the decomposition of the initially formed complex between HCO_3^- and chlorine oxide.

The analogous catalytic effect of the chloride ion is combined with the nucleophyllic effect of the hydroxyl ion in the reaction between formate and molecular chlorine.

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$$-\frac{dc}{dt} = k[HCO_2^-][Cl^+] + k'_1[HCO_2^-][HOCl] + k'_2[HCO_2^-][OH^-] + \ldots$$

At 20° $k'_1 = 8$, $k'_2 = 1 \cdot 10^5$ on the basis of previous measurements [1] is equal to 4000 in agreement with which the first term in the kinetic equation has a definite value only when the pH is as the lowest value in the range studied.

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KINETICS OF THE OXIDATION OF POLYISOBUTYLENE

A. S. Kuzminsky and N. G. Khitrova

In a series of reports [1,2] it was shown that the thermal initiation of oxidative processes for unsaturated rubbers depended upon the reaction of oxygen with double bonds located throughout the main chains of the molecule. It was also determined that the development of real conditions for the oxidation of rubber was limited by the initiation acts. In connection with this, it seemed very interesting to study the initiation mechanism for saturated polymers which lack double bonds. As models for experimentation, polyiosbutylene and butyl rubber were chosen.

EXPERIMENTAL

For purification, polyiosbutylene was dissolved in chloroform, filtered through a glass filter, and precipitated from a 2.5% solution with methanol (the chloroform and methanol were initially purified). After two reprecipitations, the polyisobutylene was dried to constant weight in vacuum. All the operations for the purification of polyisobutylene were conducted in the atmosphere.

The butyl rubber was reprecipitated from benzene. The operations for its purifications were made in nitrogen.

The study of the inhibition and free development of the autocatalytic oxidation of polymers was conducted by means of methods given by one of the authors [3,4].

The oxidation of polyisobutylene was conducted in flat-bottomed glass dishes, 30 mm in diameter and 3 mm high; 15 of such dishes, with films of polyisobutylene, were placed on a glass shelf in the reaction vessel.

In order to characterize structural changes in the polymers which occurred during the oxidation, the viscosity of solutions of the polymers was determined at various stages of the reaction. The viscosity was measured with an Ostwald viscosimeter (capillary diameter 0.3 mm) at 25°. The solutions which were used for viscosity measurements had a concentration of 0.3%.

1. Oxidation of Polyisobutylene

Fig. 1 and Table 1 contain the results of the study of the inhibited* oxidation of polyisobutylene at 110°.

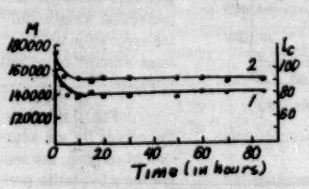


Fig. 1. The Kinetics of the consumption of the inhibitor and the decrease of the molecular weight of polyisobutylene during the process of oxidation at 110°. 1) Consumption of the inhibitor; 2) Change of the molecular weight; i_c - the free inhibitor (in %); M - the molecular weight.

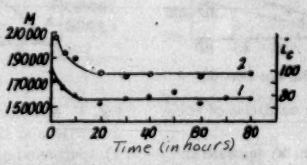


Fig. 2. The Kinetics of the consumption of the inhibitor and the decrease of the molecular weight of polyisobutylene during the process of oxidation at 130°. 1) Consumption of the inhibitor; 2) Change of the molecular weight; i_c - the free inhibitor (in %); M - the molecular weight.

As can be seen in Fig. 1 the inhibitor was only consumed during the first 5 hours of oxidation; thereafter the concentration of the inhibitor did not change. The greatest consumption of the inhibitor did not exceed 20% of

* In the rest of the text "inhibited oxidation" will mean oxidation in the presence of phenyl-β-naphthylamine (inhibitor).

its initial concentration. The molecular weight, also, decreased only 14% at the beginning of the experiment, and later on did not change at all. The consumption of the inhibitor and the decrease of the molecular weight occured simultaneously.

Fig. 2 and Table 2 contain the results of the consumption of the inhibitor and the decrease of the molecular weight for oxidation at 130°.

TABLE 1

Consumption of the inhibitor and change in the molecular weight of polyisobutylene during the oxidation at 110°.

Initial concentration of the inhibitor was 1.28 millimoles/liter (0.5%)

Oxidation time (in hours)	Inhibitor		Molecular weight $M.w.\cdot10^{-3}$
	Free (%)	Consumed (%)	
0	100.0	0	175.0
2.5	87.0	–	–
5	75.0	21.4	152.7
10	74.0	24.1	152.0
15	75.0	21.7	148.0
20	72.0	22.2	152.0
30	74.0	20.2	151.6
50	72.0	18.1	151.0
60	75.0	12.7	151.0
70	76.0	12.4	146.3
80	75.0	19.4	148.8

TABLE 2

Consumption of the inhibitor and change in the molecular weight of polyisobutylene during the oxidation at 130°.

Initial concentration of the inhibot was 1.28 millimoles/liter (0.5%)

Oxidation time (in hours)	Inhibitor		Molecular weight $M.w.\cdot10^{-3}$
	Free (%)	Consumed (%)	
0	100	0	194.0
2	90.3	10.3	207.0
5	87.2	19.6	194.0
10	79.5	25.6	180.0
20	73.0	34.1	178.0
30	93.1	21.0	174.0
40	81.5	–	177.0
50	85.5	10.5	–
60	79.1	19.3	176.0
70	82.1	23.2	160.0
80	82.8	16.4	177.0

Here, as at 110°, the consumption of the inhibitor and the decrease in the molecular weight occured simultaneously at the beginning of the experiment. The inhibitor was consumed to an extent of 25% of the initial amount.

The above changes were recorded during 20-25 hours.

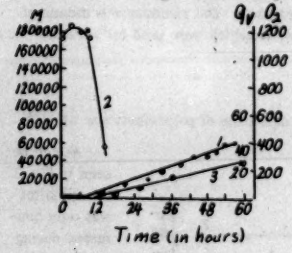


Fig. 3. Autocatalytic oxidation of polyisobutylene at 110°.

1) Addition of oxygen; 2) decrease in molecular weight; 3) separation of volatile products from the reaction; M - molecular weight; Q_V - amount of volatile reaction products (in %); O_2 - amount of added oxygen (in millimole/mole).

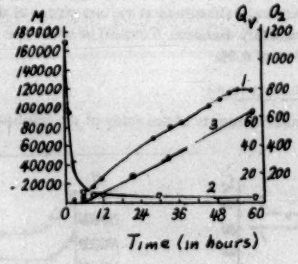


Fig. 4. Autocatalytic oxidation of polyisobutylene at 120°.

1) Addition of oxygen; 2) decrease in molecular weight; 3) separation of volatile products from the reaction; M - molecular weight; Q_V - amount of volatile reaction products (in %); O_2 - amount of added oxygen (in millimole/mole).

The free development of the autocatalytic process for polyisobutylene at all temperatures is characterized by a considerable decrease in molecular weight and the separation of a large amount of volatile products.

Fig. 3 contains the curves for the addition of oxygen, the separation of volatile products, and the decrease in the molecular weight of polyisobutylene for oxidation at 110°.

As it is seen from Figure 3 the rate of decrease in the molecular weight is proportional to the rate of oxidation. In the first stages of the reaction, a small increase in the molecular weight occurred which, however, lies within the limits of experimental error. The separation of measurable amounts of volatile products only started when the molecular weight fell to 80,000. Apparently the deep rooted decomposition did not occur in the initial polymer but in the products of its early destruction.

Figure 4 contains the curves which illustrate the oxidation of polyisobutylene at 120°. Here, the decrease in the molecular weight is more pronounced than at 110°. The molecular weight decreased 95% (from 175,000 to 10,000) in the early stages of the reaction. Again, separation of the volatile products began only after the initial fall in the molecular weight.

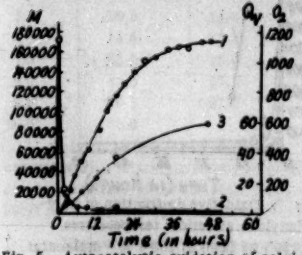


Fig. 5. Autocatalytic oxidation of polyisobutylene at 130°. 1) Addition of oxygen; 2) decrease in the the molecular weight; 3) separation of volatile products; M - molecular weight; Q_V - amount of volatile products of the reaction (in %); O_2 - amount of added oxygen (in millimoles/mole.).

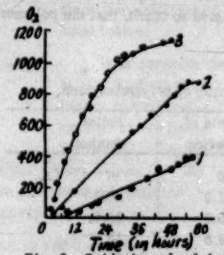


Fig. 6. Oxidation of polyisobutylene at various temperatures. 1) 110°; 2) 120°; 3) 130°; O_2 - amount of oxygen added (in millimoles/mole.).

Only a small portion (about 50 millimoles/mole) of the usual amount of oxygen, which takes part in the oxidation of the polymer, was used for the initial destruction of the molecular chain. The main part of the oxygen was used for the extensive oxidation of the fragments. This is evident from the amount of volatile products formed, which amounted to 60% of the usual weight of the polymer, and the oxygen added.

Fig. 5 contains the curves which are characteristic for the oxidation of polyisobutylene at 130°. Here, the general picture of the oxidation resembles that of the corresponding reaction at 120°. Of course, the addition of oxygen and the oxidative destruction occurred more intensively here.

Fig. 6 contains the kinetic curves for the oxidation of polyisobutylene at various temperatures. Table 3 contains the corresponding numerical data.

The change of the temperature has a great effect on the rate of oxidation of polyisobutylene. The temperature coefficient, corresponding to the stationary reaction rate, lies within the limits of 2-3. The maximum amount of oxygen used increases with the temperatures. If the maximum amount of oxygen added at 120° is 880 millimoles/mole, then at 130° the maximum amount was 1200 millimoles/mole.

Fig. 7 shows the decrease in molecular weight of polyisobutylene during oxidation at various temperatures.

TABLE 3

Kinetics of the oxidation of polyisobutylene at various temperatures

110°		120°		130°	
Time of oxidation (hours)	Consumption of oxygen (millimol/mol.)	Time of oxidation (hours)	Consumption of oxygen (millimol/mol.)	Time of oxidation (hours)	Consumption of oxygen (millimol/mol.)
7	5.9	2.75	9.0	1.50	19.3
9	29.4	5.92	49.7	3.50	106.0
13	41.0	8.92	126.5	5.50	230.0
18	76.5	11.92	176.5	7.50	336.0
21	94.0	21.67	375.0	9.50	415.0
28	135.0	28.50	480.0	12.50	540.0
33	198.0	33.50	560.0	14.50	655.0
39	258.0	36.50	630.0	16.75	705.0
43	300.0	40.50	660.0	18.25	770.0
48	312.0	46.00	755.0	21.00	860.0
51	352.0	49.00	795.0	24.00	935.0
54	386.0	52.68	840.0	27.58	1030.0
57	397.0	55.92	870.0	30.58	1045.0

TABLE 4

Amount of acids in the volatile products of the oxidative cleavage of polyisobutylene (temperature 130°)

No.	Time of oxidation (in hours)	Amount of acids, calculated at HCOOH (in %)
77	4.0	7.2
74	6.0	8.4
82	13.0	11.9
86	18.5	10.9
87	47.0	12.0

The following conclusions can be drawn from the curves in Figs. 6 and 7: 1) at all oxidation temperatures the destruction of the polymer is completed in the earlier stages of the oxidation; 2) the amount of destructive cleavage increased with the increase in the temperature. The cleavage, especially, increased at temperatures over 120°.

In the early stages of absorption of oxygen, the molecular weight of the polyisobutylene decreased so much, that the polymer no longer had technical value.

TABLE 5

Change in unsaturation in the oxidation of polyisobutylene.

No.	Temperature	Time of oxidation	Iodine number
94	130°	0	0
95	130	1.0	16.2
92	130	6.0	28.5
83	130	18.5	13.7
90	130	48.0	50.8
101	120	6.0	12.5

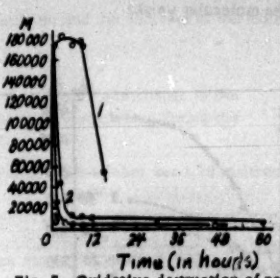


Fig. 7. Oxidative destruction of polyisobutylene at various temperatures. 1) 110°; 2) 120°; 3) 130°; M - molecular weight.

TABLE 6

Consumption of the inhibitor in the oxidation of butyl rubber at 130°. Initial concentration of the inhibitor was 25 millimoles/liter.

Elapsed time (in hours)	Free inhibitor (in %)
0	100.1
2	95.1
10	78.7
20	70.9
30	75.0
40	78.6
50	71.5
70	67.5
80	62.3

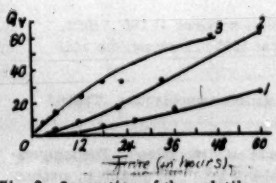


Fig. 8. Separation of the volatile reaction products during the oxidation of polyisobutylene at various temperatures. 1) 110°; 2) 120°; 3) 130°; Q_V - amount of volatile reaction products of the oxidation (in %).

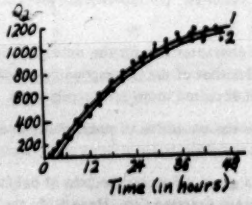


Fig. 9. Oxidation of polyisobutylene of various molecular weights at 130°. 1) Polyisobutylene molecular weight 175,000; 2) polyisobutylene molecular weight 50,000; O_2 - the amount of added oxygen (in millimoles/mole.).

Fig. 8 contains the results of the separation of volatile products in the reactions at various temperatures. The rate and the total amount of volatile products increased with the increase in temperature. Water, aldehydes, and ketones were detected in the volatile products. Characteristic results for the amount of acids formed in various stages are given in Table 4. Usually the sum of the acids formed, at the various stages of the oxidation of polyisobutylene, is around 8-12%. The amount of acids in the oxidized polymer is about 3-5%.

Only traces of peroxides were found in all the stages of the oxidation. Apparently the peroxides of polyisobutylene are unstable at higher temperatures and quickly decompose. The unsaturation of polyisobutylene is increased during the process of its oxidation (Table 5).

In a separate series, the effect of the molecular weight of isobutylene upon the kinetics of its oxidation was studied. The results of the experiments are given in Fig. 9. The kinetic oxidation curves of two forms of polyisobutylene, one of which had an average molecular weight of 50,000 and the other 175,000, are given in the figure. Both of the curves coincide satisfactorily, so that it can be said that the molecular weight of the polymer has no effect on the autocatalytic oxidation.

When polyisobutylene was heated in high vacuum, cross-linking occurred, as is shown by Figure 10.*

* The investigation of the structural changes in polyisobutylene and butyl rubber in high vacuum were conducted by A.S. Kuzminsky and I.A. Shokinim.

TABLE 7

Kinetics of the oxidation of butyl rubber at 110°

Elapsed time (in hrs.)	Oxygen consumption (in millimoles/mole)	Elapsed time (in hrs.)	Oxygen consumption (in millimoles/mole)
5.0	10.0	11.0	70.0
6.0	15.0	12.0	85.0
7.0	25.0	15.0	112.0
8.0	40.0	17.0	132.0
9.0	50.0	21.0	173.0
10.0	60.0	–	–

Oxidation of Butyl Rubber.

Figure 11 and Table 6 contain the results of the change of consumption of inhibitor in the oxidation of butyl rubber.

The curve for the consumption of the inhibitor in butyl rubber consists of two parts, AB and BC. The initial consumption is characterized by its great rapidity (part AB) but on part BC, the consumption rate of the inhibitor decreases. The autocatalytic oxidation of butyl rubber, like polyisobutylene, occurs with great rapidity.

The corresponding results are given in Figure 12 and Table 7.

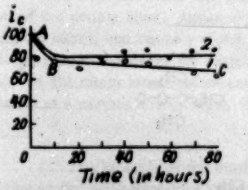


Fig. 11. Kinetics of the consumption of inhibitor in the oxidation of polyisobutylene and butyl rubber at 130°. 1) Butyl rubber; 2) polyisobutylene; i_c - inhibitor (in %).

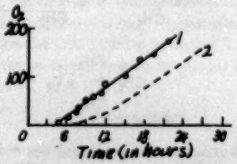


Fig. 12. Kinetics of the autocatalytic oxidation of butyl rubber and and polyisobutylene at 110°. 1) Butyl rubber; 2) polyisobutylene; O_2 - the amount of added oxygen (in millimoles/mole).

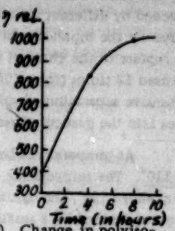


Fig. 10. Change in polyisobutylene in high vacuum at 200°. η_{rel} - the relative viscosity of benzene solutions of polyisobutylene.

As with polyisobutylene, when butyl rubber is heated in a high vacuum, cross-linking occurs.

Discussion of the Results

1. Oxidation of polyisobutylene. As shown in the experimental section, the consumption of the inhibitor occurs at the same time as the molecular weight of the polymer decreases wherein both proceed to a certain limit which varies with the temperature. Therefore, study of the inhibited oxidation of polyisobutylene leads to the conclusion that the long chains of the polymer are more reactive than the short. Oxidation of the polymer, in the presence of the inhibitor, apparently depends on the formation of peroxide radicals by the thermal decomposition of the high molecular weight fraction, and their subsequent extinction by reaction with the inhibitor. The free development of the reaction chain rapidly leads to an extensive destruction of the polymer.

An outline can be given for the initiation of the oxidation of polyisobutylene, which shows that the molecule splits and oxidizes to form peroxides. The peroxide radical, which forms as a result of the reaction, is the initial active center for the oxidation of polyisobutylene. The rate constant for the initiation of oxidation reaction of polyisobutylene (K_i), calculated from the results with the inhibitor, is equal to $1.8 \cdot 10^{-7}$ mole/liter/sec. at 110°.

If in unsaturated polymers the initiation rate constant is fully dependent upon the number of more active double bonds, which are located in the main chains of the molecule, then the value of K_i for polyisobutylene is determined by the molecular weight. As was pointed out above, the longer chains of polyisobutylene are less stable, react more easily, and as a result form the initial active centers which take part in the further development of the reaction chain. The weakness of the C-C bond in the molecular chain of polyisobutylene is the reason for its ease of oxidation.

Polyisobutylene is the most reactive of all of the saturated polymers. The ease of thermal and oxidative destruction of polyisobutylene does not allow the vulcanization of its peroxides necessary to change it to a polysilicone polymer. Conditions must be chosen for the vulcanization so that a considerable splitting of the molecule chain does not occur at the same time as the oxidation of the side methyl groups.

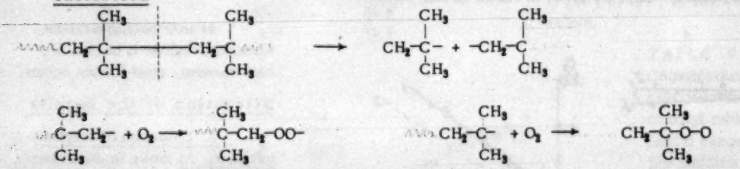
It can be shown that, in contrast, the value of the initiation constant, does not have an important effect on the kinetics of the autocatalytic oxidation. However, no real contrast exists as the free and inhibited oxidations proceed by different mechanisms. Upon comparing the curves of the decrease in the molecular weight with the curve for the separation of the volatile products, it can be pointed out that the oxidative process is accompanied by rupture of the chain of the polyisobutylene. At the beginning of the oxidation the molecular weight is decreased 10 times (from 175,000 to 2000-5000). The further destruction of the polymer is characterized by the extensive separation of volatile products so that, at the end of the experiment, 60 % of the oxidized polymer goes into the gaseous phase.

At temperatures below 100° the polymer was oxidized extremely slowly. A measurable oxidation begins at 110°. The temperature coefficient of the rate of splitting, in the 110-120° range, is equal to 3. At temperatures above 120°, the oxidative splitting occurs with an extremely small temperature coefficient (1.1 – 1.2), which is characterized by a small energy of activation.

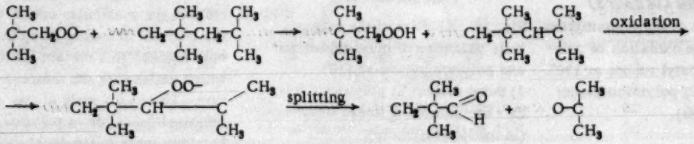
On the basis of the above experimental material, a probable outline for the oxidation of polyisobutylene was constructed.

Schema of the oxidation of polyisobutylene

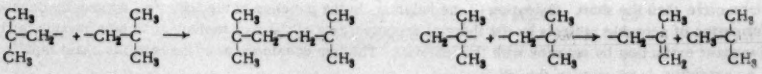
Initiation



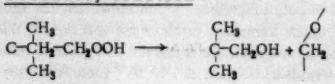
Development of the chain



Breaking of the chain



Secondary reaction



and so on according to the first chain of the scheme

The initial step of the oxidation is the formation of the peroxide radical.

The stabilization of the peroxide is undoubtedly related to the ortho-hydrogen atom of the methylene or methyl group, which, apparently, is related to the double bond formation.

2. Oxidation of butyl rubber. Butyl rubber has the properties of an unsaturated polymer and polyisobutylene. Like polyisobutylene it tends to be decomposed by heating, but its molecule contains double bonds in its main chain, which readily take part in initiation acts. Therefore, on the thermal oxidation of butyl rubber, the initial active centers will be formed by two processes: 1) by the splitting of the C–C bonds of the molecular chain, and 2) by the action of the oxygen on the double bonds of the polymer.

As shown in the experimental section, the curve for the consumption of the inhibitor consists of two parts. The beginning of the initiation occurs with great rapidity (part AB of the curve); it includes the active centers resulting from the rupture of the C–C bonds, and small amounts of those resulting from the addition of the oxygen to the double bonds. When a stable chain length of the molecule is reached, the further formation of initial active centers occurs only as a result of a thermal activation of the double bonds. Because of this, initiation for butyl rubber is characterized by two, not one, initiation constants:

K_r – the rate initiation constant of the process which proceeds by means of the C–C bonds; K_i – the rate initiation constant for the process occurring by means of the double bonds.

Calculated * from the results of the inhibited runs, the rates of the initiation of the oxidation of butyl rubber at 130° are respectively (in moles/liter/sec.):

$$K_r = 1.06 \cdot 10^{-7} \text{ and } K_i = 0.14 \cdot 10^{-7}.$$

K_i for butyl rubber is 35 times smaller than for sodium butadiene rubber. Because of this, it is the most stable of the unsaturated polymers.

It is clear that at lower temperatures, where the thermal decomposition does not as yet take place, it will be stable in relation to the degree of unsaturation. At temperatures over 100° active centers form, determined mainly by the value of K_r, which is 7 times greater than K_i.

This does not mean that ordinary bonds, at temperatures above 100°, become less stable than the π-component of the double bond. Apparently, the amount of ordinary bonds in butyl rubber exceeds the amount of double bonds 50 times, and the rate of the oxygen process is only 7 times greater than the first. Thus, it can be concluded that the rate of attack by the oxygen on the C–C position is 50:7=7.1 times slower than for the double bond position. As the chain length decreases, the process occurring by means of the C–C bonds decreases in rate and finally, at a certain chain length, it stops.

SUMMARY

1. The kinetics of the inhibited and autocatalytic oxidation of polyisobutylene and butyl rubber were studied at the temperature of 110–130°.

2. It was shown that the consumption of the inhibitor occurs concurrently with a decrease in the molecular weight of the polyisobutylene. Both of the processes occur at the same level varying with the temperature) only in the early stages of the reaction. On the basis of the above facts, it was concluded that the higher molecular weight fractions were more reactive than the lower molecular weight ones.

3. It was shown that the initiation of the oxidation of polyisobutylene occurred with the thermal cleavage of the molecular chains, which were in the high molecular weight fractions.

The initiation with butyl rubber depended as much on the rupture of the C–C bonds as on the oxidation of the double bonds. Therefore, the rate of initiation is not determined by one, but by two constants (at 130°: K_r = 1.06 mol/liter/sec; K_i = 0.14 mol/liter/sec).

4. It was shown that the free development of the oxidative process leads to a deep destruction of polyisobutylene in the early stages of the oxidation.

5. A probable schema for the reaction mechanism is given.

6. It was shown that both polyisobutylene and butyl rubber form cross-linkages when heated in a high vacuum (with a slight concentration of oxygen).

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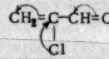
* K_i was calculated from the rate of the consumption of the inhibitor on the section BC of the curve. $K_i + K_r$ was calculated from the rate of consumption of the inhibitor on the section AB.

ACTION OF CHLOROAMIDES ON CHLOROPRENE IN AQUEOUS AND ALCOHOLIC SOLUTIONS

A. A. Petrov

Addition reactions of chloroprene, as additions between the conjugate double bond systems and polar substituents, are of great interest for the development of theories on the transformation of unsaturated compounds. The experimental material, up to now, shows the presence of radical differences in the additions of halogens, hydrogen halides, and hypohalous compounds to this substance. Chlorine adds more than 80% to the 1,4-positions of chloroprene [1], and bromine gives the 1,4 product almost exclusively [2]. Hydrogen bromide and chloride also add to the 1,4 positions to form the 4-halo-2-chlorobut-3-enes [3].

These results upheld the usual electronic formula of chloroprene; i.e., they indicated that a higher electron density was present at the first and a lower one at the fourth carbon atom:



However, with hypohalous compounds, especially with hypobromous acid [4] and alkyl hypoiodides [5], chloroprene gives almost exclusively 3,4-products. Chlorine iodide behaves in a similar way [6]. In this case, the greatest electronic density is found on the 4th carbon atom, which disagrees with the electronic theory. Therefore, it must be admitted that the order of addition is not determined, in this case, by the resulting polarization of the molecule, but by the mutual interaction of the molecules at the moment of the reaction. In relation to the preferred addition of hypohalous compounds to neighboring carbon atoms, chloroprene is not an exception. This order of addition has been found for hypohalous compounds in all experiments up to now.

The author, for example, showed that with divinyl, the ratio between the 1,2- and 1,4-products with hypochlorites, depends on the nature of the starting compound and the molecule which is adding, as well as on the temperature of the reaction system [7]. With alkyl hypobromites and alkyl hypoiodites, the formation of 1,4-compounds could not be shown in any of the cases studied [7,8].

On continuing the study of the reactions of chloroprene with hypohalous compounds, the author found that, in spite of the established rule, hypochlorous acid and alkyl hypochlorites added to chloroprene preferentially at the 1,4 positions, when aqueous or alcoholic solutions are treated with chloroamides •. Therefore, this was the first case to be found where hypohalous compounds added preferentially to the ends of a conjugated system.

Chloroprene chlorhydrin was obtained by the action of an aqueous solution of mono chlorourea in acidic media. Theoretically the six following compounds could be expected to form: five of them, chloroalcohols; one, the unsaturated chloroketone. The latter was previously obtained by the cleavage of bromine from the oxidation product of divinyl dibromide chlorohydrin [8].

$CH_2Cl{-}CCl(OH){-}CH{=}CH_2 \longrightarrow CH_2Cl{-}CO{-}CH{=}CH_2$ (I);
$CH_2Cl{-}CCl{=}CH{-}CH_2OH$ (II); $CH_2OH{-}CCl_2{-}CH{=}CH_2$ (V);
$CH_2{=}CCl{-}CHOH{-}CH_2Cl$ (III); $CH_2{=}CCl{-}CHCl{-}CH_2OH$ (VI);
$CH_2OH{-}CCl{=}CHCl$ (IV);

Distillation of the reaction products showed that, mainly, two substances were formed. The first of these, (chlorohydrin III) was extracted with water from the substances in the lower boiling fraction. The second (chlorohydrin II) was obtained in almost pure state by a simple distillation of the reaction products. The unsaturated chloroketone, which could easily be detected by its sharp odor, was not found in any quantity.

Besides the two chlorohydrins considerable amounts of products, resulting from the addition of chlorine to the chloroprene, and undistillable substances which were not investigated further, were obtained.

• The question of the mechanism of the reaction between chloroamides and olefins in aqueous and alcoholic solutions was studied in previous investigations [7].

The usual yield of the chlorohydrin was about 30%. The ratio between the first (Formula III) and the second (Formula II) chlorhydrin was 1:2/6 for the three experiments. The structure of the chlorohydrin, b.p. 75.5-76° at 20 mm, was determined by the method used previously to determine the structure of chloroprene bromohydrin [4]. The presence of the hydroxyl group was shown by acetylation with acetic anhydride. The acetate was obtained in 80% yield. The presence of a double bond was shown by bromination in chloroform with bromine. The reaction proceeded very easily and produced a liquid dibromide. The bromohydrin of similar structure gave a crystalline. The position of the hydroxyl group was determined by the oxidation of the bromide to the ketone, which gave methyl ethyl ketone upon reduction with zinc and acetic acid. Therefore, the hydroxyl group undoubtedly was tertiary in character and so only Formula (III) could be assigned to it. All of the other formulas were excluded. In connection with this formula, chlorohydrin (III) formed the previously studied chloroprene oxide by the action of bases.

The structure of the chlorohydrin, b.p. 114.5-115° at 20 mm, was determined in the following manner. The presence of a hydroxyl group was shown by acetylation with acetic anhydride which, because it was a primary hydroxyl group, went very easily. The yield of the acetate was about 90%. The acetate was easily differentiated from that of chlorohydrin (III) by its odor. The presence of a double bond was shown by bromination. The bromine added to this compound with difficulty. The reaction was not completed even after 24 hours. The yield of the dibromide was about 80%. No ketone was formed by the oxidation of this compound with the chromic mixture. Monochloracetic acid was obtained in good yield upon oxidation of the chlorohydrin with potassium permanganate. The formation of the latter is possible only with chlorohydrins (II) and (IV).

TABLE 1

Substance	Boiling point	Pressure (in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated
$CH_2=CCl-CHOH-CH_2Cl$	75.5-76	20	1.3126	1.4916	31.14	31.46
$CH_2=CCl-CH(OCOCH_3)-CH_2Cl$	89-89.5	20	1.2443	1.4650	40.68	40.83
$CH_2Br-CClBr-CHOH-CH_2Cl$	134.5-136	10	2.1002	1.5701	47.00	47.46
$CH_2Br-CClBr-CO-CH_2Cl$	124-125	10	2.0991	1.5600	46.04	45.85
$CH_2Cl-CCl=CH-CH_2OH$	114.5-115	20	1.3323	1.5100	31.66	31.46
$CH_2Cl-CCl=CH-CH_2OCOCH_3$	116.5-117	20	1.2646	1.4822	41.28	40.83
$CH_2Cl-CClBr-CHBr-CH_2OH$	142.5-143	10	2.0973	1.5740	47.33	47.46

The choice between these formulas, in favor of Formula (II) was based on the fact that two atoms of chlorine were removed by the action of zinc on the chlorohydrin in aqueous alcohol. The corresponding alcohol could not be isolated, but ethers of 1,2-butadien-4-ol could be obtained from the ethers of this chlorohydrin (see below). Therefore, formula II was adopted for the chlorohydrin by analogy with the structure of these ethers.

Table 1 contains the constants of the chlorohydrins and several of their derivatives.

A comparison of the constants of chlorohydrins (III) and (II) with the constants of analogously formed divinyl chlorohydrins, led to the following generalizations: in the case of 1,4-derivatives, as a rule the value of the molecular refractivity found is greater than the value calculated; in the case of the 1,2-derivatives, the calculated value of the molecular refractivity, as is usual for many organic compounds, is greater than that found. The presence of an exaltation with the 1,4-derivatives must be related to the decreased reactivity of the double bond in these compounds. It is also interesting to point out that the 1,4-chlorohydrin of chloroprene boiled higher than the 3,4-bromohydrin of chloroprene.

An outline of the method for the determination of the structure of the products of the reaction between chloroprene and an aqueous solution of monochlorourea is given below. (see next page)

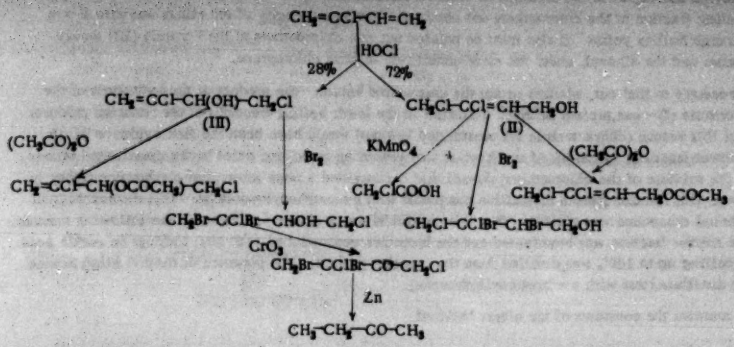
Two of the six possible chloroethers were obtained in each case by the action of N,N-dichlorophenylsulfonamide on solutions of chloroprene in methyl and ethyl alcohols.

$CH_2Cl-CClOR-CH=CH_2$ (I) $CH_2Cl-CCl=CH-CH_2OR$ (II) $CH_2=CCl-CHOR-CH_2Cl$ (III)

$CH_2OR-CCl=CH-CH_2Cl$ (IV) $CH_2OR-CCl_2-CH=CH_2$ (V) $CH_2=CCl-CHCl-CH_2OR$ (VI)

Besides the chloroether, the reaction products also included 1,2-dichloro-1,3-butadiene, chloroprene dichloride, and a very small amount of an undetermined chloroketone, formed, apparently, as a result of

Schema 1



the hydrolysis of the chloroether with Formula (II) during steam distillation of the reaction products. The formation of 1,2-dichlorobutadiene indicates that chloroprene, like benzene, can enter into substitution reactions. Small amounts of 1,2-dichlorobutadiene [1] were also formed during the chlorination of chloroprene.

The lower boiling chloroethers could not be separated from the dichlorides by distillation. They were purified, either by treatment with alcoholic alkali in the cold, or by the action of zinc dust in a heated aqueous alcoholic solution. In comparison, chloroethers were more stable than the dichloride to these reagents.

The higher boiling chloroether, which constituted about 80% of the mixture of chloroethers, was isolated in a substantially pure state by the usual vacuum distillation through a column.

The yield of the chloroethers was usually around 50%. This appeared to be the usual yield of the chloramide method.

The structure of the chloroethers was determined in the same manner as the structures of the ethers of chloroprene iodohydrin had previously been [5]. Previously reported chloralkoxyprenes, whose structure had been determined by their transformation (action of dilute H_2SO_4) into ketones which, by bromination and then reduction, were transformed into methyl ethyl ketone, obtained by warming them with alcoholic alkali. Therefore, of all the possible formulas, only formula (III) could be assigned to this substance.

Determination of the structure of the higher boiling chloroether presented greater difficulties. However, they were eliminated and a method for structure determination was found. A mixture of monochloroacetic acid and ethoxy acetic acid was obtained by the oxidation of the substance with potassium permanganate; the former in a much greater amount. This transformation made it possible to assign either Formula (II) or (IV) to the chloroether. In order to resolve this question of the structure, after a study of a series of other possibilities, the property of aliphatic dihalides containing neighboring halogen atoms, that their halogens were removed with zinc to form ethylene derivatives [10], was employed. If the halogen atoms are not side by side, the zinc reacts slowly and usually a substitution of the halogen by hydrogen occurs. The chloroethers reacted very rapidly with zinc dust in aqueous alcohol solutions to form allenic ethers, one of which had already been reported in the literature [11] as the main reaction product The formulas of these ethers corresponded with the analysis. A comparison of their constants with those of isomeric butadiene ethers, which have been fully described in the literature of the last few years, made it possible to assign to them the formula given in the outline, which was based on their method of preparation.

Besides the allenic ethers, the action of zinc on the chloroethers produced the previously described ethers of chlorocrotonyl alcohol [3]; i.e. a large amount of the more active chlorine atom was reduced. The formation of similar side products has been frequently reported in the literature. Chloroprene was another side product. The yield of chloroprene was sharply reduced upon going from methyl to ethyl, to butyl ethers. The formation of chloroprene can be explained by the 1,4-elimination of the halogen and the alkoxyl group.

Therefore, no indication of the presence of other substances, outside of the chloroethers of Formula (II), in the higher boiling fraction of the chloroethers was obtained. The homogeneity of the ethers was also shown by their narrow range boiling points. It also must be pointed out that chloroethers of the Formula (III) slowly eliminated chlorine and the alkoxyl, under the same conditions, to form chloroprene.

It was necessary to find out, whether or not the unsaturated ketone – the product of the hydrolysis of the chloroether of Formula (I) – was present in small quantities in the lower boiling fractions of the reaction products. The sharp odor of this ketone (characteristic for unsaturated ketones) would have been the first evidence of its presence in the lower fractions. Analysis of the fraction, corresponding in boiling point to the unsaturated ketone, (less than 2% of the mixture of the chloroethers) showed that it contained a large amount of a substance richer in chlorine. However, this fraction gave a crystalline compound with p-nitrophenylhydrazine. This showed beyond doubt that a carbonyl compound was present. That this compound was a ketone was shown in the following manner. The whole of the narrow fraction was brominated and the bromides were reduced with zinc turnings in acetic acid. Then a portion, boiling up to 100°, was distilled from the reaction product. The presence of methyl ethyl ketone was shown in the distillate (test with p-nitrophenylhydrazone).

Table 2 contains the constants of the ethers obtained.

TABLE 2

Substance	B.p.	Pressure (in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated
$CH_2=CCl-CHOCH_3-CH_2Cl$	58-59°	20	1.1710	1.4612	36.37	36.20
$CH_2=CCl-CHOC_2H_5-CH_2Cl$	67.5-68	20	1.1297	1.4562	40.89	40.82
$CH_2Cl-CCl=CH-CH_2OCH_3$	80-81	20	1.2177	1.4788	36.09	36.20
$CH_2Cl-CCl=CH-CH_2OC_2H_5$	90-90.5	20	1.1683	1.4734	40.62	40.82
$CH_2Cl-CCl=CH-CH_2OC_4H_9$	119-120	20	1.0883	1.4672	50.27	50.05
$CH_2Cl-CClBr-CHBr-CH_2OC_2H_5$	127-129	10	1.8134	1.5312	56.12	56.82

TABLE 3

Substance	B.p. (at 755-760 mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Literature reference
$CH_2=C=CH-CH_2OCH_3$	87.5-87.8	0.8327	1.4395	26.60	26.00	–
$CH_3-C\equiv C-CH_2OCH_3$	87-89	–	–	–	–	[11]
$CH_2=C=CH-CH_2OC_2H_5$	107.5-107.8	0.8228	1.4389	31.36	30.62	–
$CH_2=C=CH-CH_2OC_4H_9$	153.5-154	0.8270	1.4432	40.47	39.85	–
$CH\equiv C-CH_2-CH_2OC_2H_5$	104	0.8273*	1.4148*	29.73	29.49	[12]
$CH_3-C\equiv C-CH_2OC_2H_5$	119-120	0.8363	1.4290	30.25	29.49	[13]
$CH_2=CH-CH=CHOC_2H_5$	37-38 (at 41 mm)	0.8205	1.4671	33.19	30.19	[14]

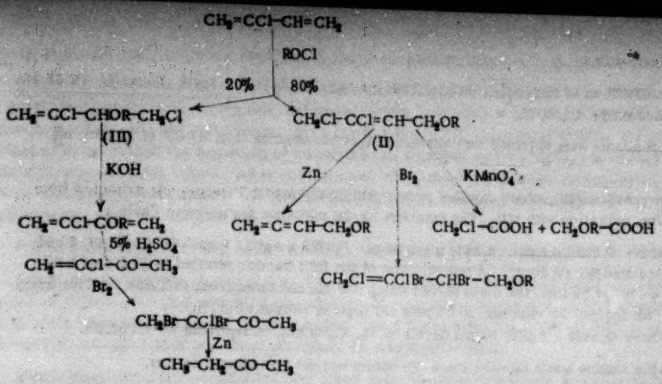
In contrast to the chlorohydrins, the 1,4-chloroethers do not give exaltations in the molecular refractivity, even though the double bonds are less reactive than in the chlorohydrins.

Table 3 lists the constants of the allenic ethers. The constants are given in this table for all of the isomeric primary ethyl ethers obtained up to now. It is seen from this table, that the highest boiling points and densities are given by ethers of acetylenic alcohols with a central triple bond. The largest refractive index is given by the conjugated diene ether. This ether gives a considerable amount of exaltation in the molecular refractivity. The great differences in the values of the refractive indices of the isomeric ethyl ethers are outstanding. The same properties were found for the methyl ether series.

An outline for the determination of the structure of the chloroethers formed by the action of the dichloroamide on chloroprene, in alcoholic solutions, is given below: (see top of next page)

In conclusion, it is necessary to discuss certain theoretical considerations relating to the properties found. From the results of the above studies, it was, first of all shown that the point of the initial attack in the reaction

* At 22°



between chloroprene and the hypohalous compounds depends on the nature of the halogen. The first carbon atom served as the initial point of attack with hypochlorous acid, and the reaction was completed at the 4 position. Thus the chloroprene molecule reacted as a conjugated system. With hypobromous acid and with hypoiodite esters, the initial point of attack was the 4 carbon atom, and the reaction was completed at position 3. A conjugated system was not present. The addition occurred at the unsubstituted, more reactive, double bond.

Therefore, the addition of hypochlorites occurred in the same manner as the addition of the halides. The order of addition for hypobromous and hypodiodous compounds was different from the order of the addition of the halides. Chlorine iodide added in the same order as the hypoiodous compounds. This new property can be explained by the presence of steric hindrance to the addition of bromine and iodine to the first position. Since position one is hindered, these halides added instead to the unsubstituted double bond.

It can be supposed that chloroprene can polarize like a conjugated system, in the presence of the poles of the corresponding hypochlorite compound, to give the maximum electron density at position one. This results in 1,4-addition. With hypobromous and especially hypoiodous compounds, this polarization does not occur, and the addition proceeds in the same manner as in a system of two isolated double bonds, one of which is more active than the other; 3,4-addition results.

It must be pointed out that the results of the hypochlorination of chloroprene are new experimental proofs of the ability of conjugated systems to add 1,4 preferentially. In fact, in the case of chloroprene, the 1,2 addition cannot occur at all and therefore cannot be the source of the 1,4 product.

EXPERIMENTAL

Action of an aqueous solution of monochlorurea on chloroprene. Freshly distilled chloroprene (177 g – (two-fold excess) was shaken for 1 hour, with cooling (until ice crystals formed) and acidification with H_2SO_4 (until 2% H_2SO_4 content), with a solution of monochlorurea, obtained by passing chlorine at –10–0° into a solution of 60 g of urea in 450 ml of water with 60 g of copper carbonate until an increase in weight of 50 g, and almost complete solution of the copper carbonate occurred. The oil was separated from the aqueous solution, dried with Na_2SO_4, and distilled, at first in a slight vacuum, and then at 20 mm. A small amount of the reaction products was extracted from the water and added to the main part of the substances. Results of the distillation:

1) 55-65° –70 g; the rest at 20 mm: 2) to 70° –4.0 g; 3) 70-80° –28.8 g; 4) 80-110° –5.4 g; 5) 110-120° –32.0 g; 6) 120-140° –4.5 g; 7) nondistillable residue –45 g.

The first fraction was unreacted chloroprene. The third fraction, according to analysis for chlorine, consisted of chloroprene chlorohydrin considerably contaminated with dichlorides. The chlorohydrin was extracted from this fraction with water. 27.8 g of the 70-80° fraction and 700 ml of water (100 ml portions) were used for the extraction. The last extraction did not give any decrease in the weight of the oil, which was equal to 15.1 g. Analysis of the residual oil for chlorine and determination of its constants showed that chloroprene

dichloride was being dealt with.

B.p. (main part 67-69° at 10 mm; n_D^{15} 1.5145. 0.1546 g substance: 0.4136 g AgCl. Found %: Cl 66.18. $C_4H_6Cl_2$. Calculated %: Cl 66.73.

The following constants were obtained for chloroprene 1,4-chlorohydrin: b.p. 67-69° at 10 mm, n_D^{15} 1.5121.

9.7 g of the chlorohydrin (III), which distilled almost completely over a 1° range, was extracted from the aqueous solution after saturation with salt. The constants for the substance are given in Table 1.

0.1904 g substance: 0.3886 g AgCl. 0.1844 g substance: 0.3728 g AgCl. Found %: Cl 50.49, 50.01 $C_4H_6OCl_2$. Calculated %: Cl 50.29. A redistillation of the fifth fraction resulted in 26.5 g of a substance, b.p. 114-116° at 20 mm, the main part of which had the constants given in Table 1. This fraction was shown, by analysis for chlorine, to be pure chloroprene chlorohydrin (III).
0.1572 g substance: 0.3198 g AgCl. Found %: Cl 50.32. $C_4H_6OCl_2$. Calculated %: Cl 50.29.

The nondistillable residue was a tar-like mass. Its nature was not investigated further.

Thus 35.2 g of the pure chlorohydrins (III) and (II) or 25% of theory was obtained from 1 mole of monochlorurea. The ratio between the amount of the chlorohydrin (III) and (II) was 1:2.6. If the amount of the chlorohydrins in the intermediate fractions was taken into account, the yield would be about 30%.

The acetylation of the chlorohydrins was effected with the aid of 150% acetic anhydride and a drop of H_2SO_4. When the H_2SO_4 was added, the reaction mixture was cooled to keep the temperature from exceeding 40°. The yield of the acetate of chlorohydrin (III) was 82% and that of (II), 89%. The constants of the acetates are given in Table 1.

Chlorohydrin (III) acetate: 0.1610 g substance: 0.2552 g AgCl. Found %: Cl 39.21. $C_6H_8O_2Cl_2$. Calculated %: Cl 38.74.

Chlorohydrin (II) acetate: 0.1852 g substance: 0.2908 g AgCl. Found %: Cl 38.84. $C_6H_8O_2Cl_2$. Calculated %: Cl 38.74.

Chlorohydrin (III) acetate has a more intense pleasant odor.

Bromination of the chlorohydrins was effected with equivalent amounts of bromine in chloroform. Chlorohydrin (III) added bromine readily; decolorization of the solution occurred in a few minutes and was accompanied by the evolution of heat. A yield of 13.5 g—82% of the bromide was obtained from 7.7 g of the chlorohydrin.

0.1950 g substance: 0.4312 g AgCl + AgBr. Found %: Cl + Br 77.05. $C_4H_6OCl_2Br_2$. Calculated %: Cl + Br 76.70.

Chlorohydrin (II) added bromine slowly; decolorization of the solution occurred only on the next day. A 7 g—78% yield—of the dibromide was obtained from 4.2 g of chlorhydrin (II).

0.1646 g substance: 0.3656 g AgCl + AgBr. Found %: Cl + Br 77.39. $C_4H_6OCl_2Br_2$. Calculated %: Cl + Br 76.70.

Both of the dibromides were viscous, slightly yellow liquids with a pinelike odor.

Oxidation of chlorohydrin (III) dibromide. 10 g of 80% H_2SO_4 was added dropwise, with mechanical stirring and cooling (15-20°), to a solution of 10 g of chlorohydrin (III) dibromide and 5 g of sodium dichromate in 30 ml of 80% acetic acid. After 2 hours of stirring, the mixture was diluted with water, the ketone was separated, washed with aqueous sodium carbonate, and dried with $CaCl_2$. The last operations were best conducted with a solution of the ketone in ether. A 8.7 g—88% yield, of the ketone was obtained. The constants are given in Table 1.

0.1889 g substance: 0.4200 g AgCl + AgBr. Found %: Cl + Br 77.47. $C_4H_6OCl_2Br_2$. Calculated %: Cl + Br 77.22.

The ketone was a yellow, lively liquid with a characteristic sour, somewhat irritating odor. It was easily reduced to methyl ethyl ketone with zinc in acetic acid. Methyl ethyl ketone was steam distilled from the

reaction mixture and analyzed in the distillate, as the p-nitrophenylhydrazone, m.p. 122-124°.

Oxidation of chlorohydrin (II). 29 g of potassium permanganate was added, in small portions over a 2 hour period with mechanical stirring and cooling (to 15-20°), to a mixture of 7.1 g of chlorohydrin (II), 20 g of magnesium sulfate, and 150 ml of water. After the filtration of the manganese dioxide, the solution was evaporated in vacuum until the beginning of crystallization, acidified with 5% H_2SO_4 and treated with ether until the extraction of acids ceased. After distillation of ether, chloroacetic acid, contaminated by a small amount of oxalic acid, from which it was purified by distillation, remained in the flask. The yield of the monochloroacetic acid was 3.5 g or 75%.

0.1828 g substance: 0.2779 g AgCl. Found %: Cl 37.61. $C_2H_3O_2Cl$. Calculated %: Cl 37.53.

Action of alkali on the chlorohydrins. The previously reported chloroprene oxide was obtained by the distillation of chlorohydrin (III) over KOH (the chlorohydrin was added dropwise to an 80% solution of KOH heated to 150°). The yield, from 5 g of chlorohydrin, was 3.0 g or 80%. B.p. 109-111°, n_D^{20} 1.4594. A b.p. of 109.4-109.6° and n_D^{20} 1.4592 was found previously for chloroprene oxide.

When chlorohydrin (II) was distilled over alkali under the same conditions, a tarring of the substance occurred. 0.5 g of a liquid distillate, n_D^{20} 1.4795, was obtained from 7 g of the chlorohydrin; it was not investigated any further.

Action of N,N-dichlorophenylsulfonamide on methyl alcohol solutions of chloroprene. 126 g of N,N-dichlorophenylsulfonamide (90% activity) was added in small portions, with mechanical stirring and cooling to a temperature of +4-6° with a freezing mixture to 132 g of freshly distilled chloroprene (several fold excess) in 300 ml of ethyl alcohol. The mixture was stirred for 1 hour after the addition of the chloroamide. A test with acidified KI solution showed that no active chlorine was present in the solution. The chloroethers were steam distilled until the oily droplets disappeared from the distillate. 75.8 g of phenylsulfonamide was extracted from the residue with hot water. There then remained 13 g of a tarry substance, which probably was the thermally changed addition products of chloroamide and chloroprene.

The reaction products, separated from unreacted chloroprene, were vacuum distilled at 20 mm:

1) to 50° –3.2 g; 2) 50-60° –19.0 g; 3) 60-70° –3.4 g; 4) 70-78° –2.1 g; 5) 78-83° –59 g; 6) 83-100° –3.2 g; 7) residue, 8 g.

Analysis of the 50-60° fraction showed that it consisted of a mixture of chloroprene chloroether and dichloride. To remove the dichlorides, the fraction was treated in the cold, with 10% alcoholic KOH until an alkaline reaction was obtained. 30% of the KOH, equivalent to one chlorine atom, was consumed. After such a treatment, the ether boiled over a narrower range (57-60° at 20 mm). However, it still contained some of the chloride.

0.1964 g substance: 0.3896 g AgCl. Found %: Cl 49.07. $C_8H_8OCl_2$. Calculated %: Cl 45.74.

This fraction was used for the determination of the structure of the main product without further purification.

The fraction was treated with zinc dust in aqueous alcohol for the preparation of the pure chloroether. After boiling for 30 min., the reaction products were steam distilled, separated, dried, and vacuum distilled. The substance with the constants given in the table was obtained in this manner.

0.1728 g substance: 0.3167g AgCl. Found %: Cl 45.34. $C_8H_8OCl_2$. Calculated %: Cl 45.74.

50 g of a substance, b.p. 80-81° at 20 mm, and other constants, given in Table 2, was obtained by the redistillation of the fifth fraction.

0.1822 g substance: 0.3420 g AgCl. Found %: Cl 46.43. $C_8H_8OCl_2$. Calculated %: Cl 45.74.

Thus, the total yield of the chloroethers, if the intermediate fractions were taken into account, was about 80 g or 52%. The ratio between chloroether (III) and (II) = 1:3.5.

Action of alcoholic alkali on the chloromethyl ether (III). 7.8 g of the chloromethyl ether (III) was added through the reflux condenser to a boiling solution of 5.6 g of KOH in 25% alcohol. After 30 minutes of refluxing, the reaction products were steam distilled. 4 g of chloromethoxyprene, b.p. (main fraction) 58-59.5° at 85 mm, d_4^{20} 1.0681, n_D^{20} 1.4732., was obtained. Previously the constants: b.p. 58.5-59.5°, d_4^{20} 1.0579, n_D^{20} 1.4712, were obtained for this substance. When the substance was hydrolyzed by shaking with 5%

When the substance was hydrolyzed by shaking with 5% H_2SO_4, the previously reported ketone, 38-40° at 30 mm, was obtained.

Action of alcoholic alkali on chloromethyl ether (II). 10.5 g of chloromethyl ether (II) was added in small portions to a solution of 4 g of NaOH in 25 ml of methyl alcohol, and the mixture was refluxed for 30 min. on the water bath. 4.3 g of NaCl, as compared to the calculated 4 g, precipitated. Upon distillation of the reaction mixture, 5 g of a substance, which boiled mainly at 68-72°, d_4^{20} 1.0228, n_D^{20} 1.4440, was obtained. The substance contained a lower percent of chlorine than was required for chloroerythroglycol dimethyl ether.

0.1475 g substance: 0.0958 g AgCl. Found %: Cl 16.07. $C_6H_{11}O_2Cl$. Calculated %: Cl 23.54.

Action of zinc on an aqueous alcoholic solution of the chloromethyl ether (II). Chloromethyl ether (II) was added, dropwise through the side arm, into a flask containing 30 g of zinc dust in 100 ml of 70% alcohol, while the mixture was being continuously distilled through a 30 cm herringbone dephlegmator. A violent reaction took place, forming substances which were readily separated from the distillate by mixing with a $CaCl_2$ solution. After separation of the reaction products, the solution was distilled once more, and some more of the substances were obtained from the first part of the distillate. A total of 17.2 g of an oil was obtained which, on redistillation through a 30 cm dephlegmator, was readily separated into the following fractions: 1) 55-65° –2.6 g; 2) 65-87.25° –2.1 g; 3) 87.25–87.75° –62 g; 4) 87.75–100° –1.0 g; 5) residue –3.6 g.

The first fraction was chloroprene. The characteristic condensation product, m.p. 173-175°, was obtained by heating the substance with a benzene solution of maleic anhydride in a sealed ampoule on the water bath, and processing it in the usual manner.

The third fraction was the allenic ether previously reported by Carothers. The constants for the substance are listed in Table 3. Analytical results: 0.1428 g substance: 0.3722 g CO_2; 0.1201 g H_2O. Found %: C 71.11; H 9.41. C_6H_9O. Calculated %: C 71.39; H 9.59.

The yield of the allenic ether was about 40%.

The residue of the redistillation was not investigated. By analogy with the residue of the redistillation of the corresponding allenic ethyl ether (see the following paragraph), it probably contained the methyl ether of chlorocrotonyl alcohol.

It must be pointed out that the chloroether (I) remained unchanged under these conditions.

Action of N,N-dichlorophenylsulfonamide on solutions of chloroprene in ethyl alcohol. 186 g of N,N-dichlorophenylsulfonamide was added to a solution of 250 g of chloroprene in 650 ml of 98% ethyl alcohol, under the conditions given above in the experiment with methyl alcohol. At the end of the addition, the mixture was stirred for 4 hours, after which a test with KI showed that only insignificant amounts of active chlorine were present. Upon distillation of the mixture of chloroethers and side products, the following fractions were obtained: 1) 47-49° at 85 mm –1.8 g; the rest at 20 mm: 2) to 60° –5 g; 3) 60-70° –26.5 g; 4) 70-80° –5 g; 5) 80-89° –5 g; 6) 89-91° –95 g; 7) 91-100° –5.8 g, 8) residue –10.5 g.

In addition, 119.1 g of the amide and 44 g of a residue, which did not steam distil, were obtained.

The first fraction was the previously reported 1,2-dichlorobut-1,3-dien: d_4^{15} 1.1993; n_D^{15} 1.5078.

0.1444 g substance: 0.3304 g AgCl. Found %: Cl 56.60. $C_4H_4Cl_2$. Calculated %: Cl 57.67.

Literature data: b.p. 46.75-47.5° at 85 mm; d_4^{15} 1.1992; n_D^{15} 1.5078.

The fraction possessed lachrymatory activity, which indicated that it contained the unsaturated chloroketone, $CH_2Cl–CO–CH=CH_2$. However, its constants and chlorine content differed widely from those of the ketone. A portion, corresponding to the unsaturated ketone by virtue of its b.p., was separated from this fraction. It had the following constants: b.p. 69-70° at 60 mm, d_4^{20} 1.2341, n_D^{20} 1.4788.

0.1520 g substance: 0.3256 g AgCl. Found %: Cl 52.99. C_6H_8OCl. Calculated %: Cl 33.92.

According to the literature, the unsaturated ketone has the following constants:

b.p. 70° at 60 mm; d_4^{20} 1.2604; n_D^{20} 1.4675.

The presence of the unsaturated chloroketone was shown, finally, by the preparation of crystalline derivatives with semicarbazide and p-nitrophenylhydrazine. The p-nitrophenylhydrazone charred at 110°.

The fraction was also treated with an excess of bromine in chloroform, and the product obtained, was boiled with zinc turnings in acetic acid for 30 minutes. It was distilled, and the portion boiled up to 100° contained methyl ethyl ketone, since it formed the characteristic p-nitrophenylhydrazone, m.p. 122-124°, with p-nitrophenylhydrazine in acetic acid.

The third fraction was a mixture of the chloroether (II) and chloroprene dichloride.

d_4^{20} 1.1814; n_D^{20} 1.4665. 0.1880 g substance: 0.3450 g AgCl. Found %: Cl 45.39. $C_6H_{10}OCl_2$. Calculated %: Cl 41.95.

If this substance did not contain any impurities other than the dichloride, then it was a mixture 86% chloroether and 14% dichlorides.

A purified chloroether was obtained by treatment with alkali.

B.p. 66-69° at 20 mm; d_4^{20} 1.1419; n_D^{20} 1.4588.

0.1566 g substance: 0.2774 g AgCl. Found %: Cl 43.82. $C_6H_{10}OCl_2$. Calculated %: Cl 41.95.

This product was used without further purification for determination of the structure of the chloroether (III). The pure chloroether (III) was obtained by treating the fraction with zinc dust in the same manner as in section 8. The constants are listed in Table 2.

0.1807 g substance: 0.3062 g AgCl. Found %: Cl 41.91. $C_6H_{10}OCl_2$. Calculated %: Cl 41.95.

The sixth fraction, on redistillation, gave 85 g of a substance, b.p. 90-90.5° and other constants listed in Table 2.

0.1596 g substance: 0.2404 g AgCl. Found %: Cl 42.59. $C_6H_{10}OCl_2$. Calculated %: Cl 41.95.

The analytical results showed that the fraction was almost pure chloroether (II). It was used for the structure determination without further purification.

Therefore, the yield of the chloroethers, if the intermediate fractions were taken into account, was 126 g or 50% of theory (calculated for 90% N,N-dichlorophenylsulfonamide).

The ratio of the chloroethers (III) and (II) = 1:4.

Action of alcoholic alkali on the chloroether (III). 10 g of the chloroether (III) was added through the reflux condenser to a solution of 7 g of KOH in 40 ml of ethyl alcohol. The mixture was refluxed for 1 hour on the water bath. The reaction products were steam distilled. In this way, 5.8 g of an oil (74% yield), a large part of which boiled at 74-75° at 85 mm, d_4^{20} 1.0155, n_D^{20} 1.4652 was obtained.

0.1652 g substance: 0.1802 g AgCl. Found %: Cl 26.98. C_6H_9OCl. Calculated %: Cl 26.74.

The constants: b.p. 74.5-75° at 85 mm, d_4^{20} 1.0152, n_D^{20} 1.4641.

The substance was easily hydrolyzed to a ketone with b.p. 38-40° at 30 mm.

Bromination of the chloroether (II). The chloroether (II) reacted very slowly with bromine. When 7.5 g of the chloroether and an equivalent amount of bromine were allowed to stand together, almost complete decolorization was obtained only after several days; hydrogen bromide was evolved. As a result of this reaction, after the removal of the chloroform, 8 g (55% yield) of a substance, whose constants are given in the Table, was obtained.

0.1540 g substance: 0.3064 g AgCl + AgBr. Found %: Cl + Br 69.32. $C_6H_{10}OCl_2Br_2$. Calculated %: Cl + Br 70.16.

Action of zinc on the chloroether (II) in aqueous alcohol. 45 g of the chloroether (II) was added, under the conditions given for the methyl ether, to 40 g of zinc dust in 150 ml of boiling alcohol. After processing the distillate in the usual manner, 20 g of a substance, which was separated into the following fractions, was obtained: 1) 55-56° –1.4 g; 2) 65-107° –2.0 g; 3) 107-108° –0.5 g; 4) 108-125° –1.0 g; the rest at 25 mm: 5) to 52° –0.6 g; 6) 52-54° –2.0 g; 7) 54-70° –1.0 g; 8) residue –0.5 g.

The first fraction was chloroprene.

The third fraction – the ethyl ether of butadien-2,3. Yield –42%. The constants for the substance are listed in Table 3. Analytical results: 0.2502 g substance: 0.6698 g CO_2; 0.2336 g H_2O. Found %: C 73.06; H 10.45. $C_8H_{14}O$. Calculated %: C 73.42; H 10.27.

The sixth fraction was the previously reported ether of chlorocrotonyl alcohol. The yield was about 6%. Found for it: d_4^{20} 0.9843, n_D^{20} 1.4405.

0.1706 g substance: 0.1822 g AgCl. Found %: Cl 26.42. $C_6H_{11}OCl$. Calculated %: Cl 26.34.

The sixth fraction was the previously reported chlorocrotonyl ether with b.p. 52.5-53.5° at 25 mm, d_4^{20} 0.9832, n_D^{20} 1.4395.

Oxidation of the chloroether (II). 38 g of potassium permanganate was added, in small portions with continuous stirring and water cooling to 15-25°, to a mixture of 17 g of the chloroether in 150 ml of water. The last portions of permanganate were decolorized slowly.

After processing in the usual manner, 8.8 g of acids was obtained. A large portion of this substance crystallized.

An analysis of the mixture showed that it consisted of 76.5% chloroacetic acid (yield 70%) and 22.5% of ethoxyacetic acid (yield 18%).

0.1631 g substance: 0.1892 g AgCl. Found %: $CH_2ClCOOH$ 76.48. 0.2249 g substance: 0.1140 g AgI (Zeisel). Found %: $CH_3(OC_2H_5)COOH$ 22.47.

The crystalline acid was filtered, recrystallized from water, and analyzed. M.p. 61°.

0.1742 g substance: 0.2626 g AgCl. Found %: Cl 37.29. $C_2H_3O_2Cl$. Calculated %: Cl 37.53.

In addition to the acids reported, oxalic acid was also formed during the oxidation (m.p. 189°).

Action of N,N-dichlorophenylsulfonamide on solutions of chloroprene in butyl alcohol. 94 g of liquid products, 76 g of the amide, and 26 g of chloroamide-chloroprene addition products were obtained by the action of 120 g of N,N-dichlorophenylsulfonamide on a solution of 130 g of chloroprene in 300 g of butyl alcohol. Two main fractions were obtained on the redistillation of the liquid products: (at 20 mm): 1) 85-90° –9 g; 2) 117-122° –55 g.

The analysis and the determination of the constants of the first fraction showed that it contained a considerable amount of products richer in chlorine than the chloroethers. Found: d_4^{20} 1.2137, n_D^{20} 1.4830.

0.1816 g substance: 0.3760 g AgCl. Found %: Cl 51.22. $C_8H_{14}OCl_2$. Calculated %: Cl 35.98.

This fraction was not investigated further.

A large part of the second fraction came over at 119-120° (20 mm) and had the constants given in Table 2. This fraction contains a somewhat lower percent of chlorine than is required for the chloroether. It could not be purified further.

0.1846 g substance: 0.2605 g AgCl. Found %: Cl 34.91. $C_8H_{14}OCl_2$. Calculated %: Cl 35.98.

Action of zinc on the chlorobutyl ether (II) in aqueous alcohol. 11.2 g of the allenic ether (yield 45%) and 3.9 g of chlorobutenol ether (13%) were obtained by the action of 40 g of zinc dust in 200 ml of ethyl alcohol (75%) on 39.5 g of chlorobutyl ether (II) (fraction 117-122° at 20 mm).

The constants of the allenic ethers are listed in Table 3. The analytical results are as follows:

0.1922 g substance: 0.5353 g CO_2; 0.1942 g H_2O. Found %: C 76.01; H 11.31. $C_8H_{14}O$. Calculated %: C 76.14; H 11.19.

The chlorobutenol ether boiled at 86-92° at 25 mm and had d_4^{20} 0.9656, n_D^{20} 1.4432.

0.1706 g substance: 0.1447 g AgCl. Found %: Cl 20.98. $C_8H_{15}OCl$. Calculated %: Cl 21.80.

The following constants were previously found for this ether: b.p. 86.75-88.5° at 25 mm, d_4^{20} 0.9595, n_D^{20} 1.4442.

SUMMARY

1. The action of an aqueous solution of monochlorurea on chloroprene was studied. The formation of two chlorohydrins: $CH_2=CCl-CHOH-CH_2Cl$ and $CH_2Cl-CCl=CH-CH_2OH$ in a ratio of 1:2.6 was obtained. The acetate, dibromide, and oxide were obtained from the first, and the acetate and dibromide from the second. The structure of the first chlorohydrin was determined by transforming it into methyl ethyl ketone, the structure of the second — by oxidizing it to monochloroacetic acid.

2. Two ethers in a ratio of 1:4, corresponding in structure to the two chlorohydrins listed above, were obtained in each case by the action of N,N-dichlorophenylsulfonamide on solutions of chloroprene in methyl, ethyl, and butyl alcohols. The structures of the lower boiling ethers were determined by transforming them into chloroalkoxyprenes: the structure of the isomeric chloroethers was determined by oxidizing them to monochloroacetic acid and reducing them to the allenic ethers.

3. The present investigation showed the presence of basic differences in the order of addition to chloroprene hypochlorous acid and its esters, and the addition of hypobromous acid hypoiodite esters.

The above differences are of considerable interest for theoretical organic chemistry.

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SYNTHESIS OF ALIPHATIC ORGANO-ELEMENTAL COMPOUNDS BY THE DIAZO METHOD

I. SYNTHESIS OF COMPOUNDS WITH THE GROUP V ELEMENTS — ORGANO-ANTIMONY, ARSENIC, AND BISMUTH COMPOUNDS

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The reaction between the metallic halides and the aliphatic diazo compounds was studied for $CuCl_2$, $CaCl_2$, $MnCl_2$, $MgCl_2$, $NiCl_2$, $FeCl_3$, $SbCl_4$, $ZnCl_2$, and $PtCl_4$ [1,2]. All of these halides catalyzed the decomposition of diazomethane; the reduction to the free metal occurred only with mercuric chloride. This had been previously found for silver salts [3]. However, it was shown [4] that α-haloalkyl-mercury compounds were formed by the reaction of diazomethane and phenyldiazomethane with the halogen salts of mercury; mercuric chloride was shown to react analogously with diazoacetic ester by Nesmeyanov and Povkh [5]. Attempts, by a series of investigators, to obtain organic derivatives of zinc [6], iron, tin [7], and phosphorus [8] by means of aliphatic diazo compounds ended in failure. Therefore, one could have concluded that the aliphatic diazo compounds, in contrast to the aromatic, cannot be used for the synthesis of various organo-elemental compounds, and the synthesis of organomercury compounds was a chance occurrence — an exception.

Since one of the authors had previously prepared aliphatic organoarsenic compounds by means of the diazo method [9], a detailed study was undertaken in order to determine the possibility of and establish the conditions for the synthesis of various organo-elemental compounds by the diazo method. The results of studies on the synthesis of organo-antimony, arsenic, and bismuth compounds are reported in this paper.

The methods for the synthesis of organoantimony compounds are very limited, and the number of known compounds of this series is small. Still smaller is the number of antimony alkyls containing substitutions in the radical. Only recently was the synthesis and properties of chlorovinyl antimony derivatives reported by Nesmeyanov and Borisov [10].

Organic and inorganic antimony chlorides are both very readily hydrolyzed so that experimentation with antimony derivatives is greatly complicated, especially, with aliphatic diazo compounds, which are so sensitive to the hydrogen halides. Nevertheless, it was possible to prepare chloromethyldichlorostibine and tri-(chloromethyl)-stibine from antimony trichloride and diazomethane, under the conditions given below, in satisfactory yields. The formation of chloromethyldichlorostibine from antimony trichloride and diazomethane (1:2) proceeds according to the scheme:

$$SbCl_3 + CH_2N_2 \longrightarrow ClCH_2SbCl_2 + N_2.$$

Tri-(chloromethyl)-stibine was obtained by the reaction of chloromethyldichlorostibine (1 mole) with excess diazomethane (3 moles):

$$ClCH_2SbCl_2 + 2CH_2N_2 \longrightarrow (ClCH_2)_3Sb + 2N_2.$$

Tri-(chloromethyl)-stibine, in contrast to other tertiary alkylstibines, is relatively stable in the air, but it slowly oxidizes and the substance clouds up as a result of the formation of the oxide. It does not react with water under the usual conditions, but on prolonged contact, (12-14 hours), the formation of a white precipitate occurs, apparently, as a result of hydrolysis and the formation of antimony oxides. The corresponding dibromide, which crystallizes readily in the form of red, shiny needles, is formed by the action of bromine on trichloromethyl antimony.

Di-(α-chloroethyl)-chlorostibine is readily formed by the reaction of trichlorostibine with diazoethane (1:2). This substance is somewhat more easily oxidized by atmospheric oxygen than trichloromethylstibine, but all are much more stable compounds when compared to the unsubstituted alkylstibines. Apparently, the presence of the chlorine atom in the α-position considerably decreases the tendency for the alkylstibines to be oxidized. This conclusion was supported by the fact that the formation of the acid was completed only after 15-20 hours when di-(α-chloroethyl)-chlorostibine was acted upon by hydrogen peroxide.

Antimony pentachloride does not form organoantimony compounds with diazomethane; the reduction of the pentavalent to the trivalent antimony takes place according to the reaction:

$$SbCl_5 + CH_2N_2 \longrightarrow SbCl_3 + CH_2Cl_2 + N_2.$$

Therefore, various α-haloalkyl derivatives of antimony can be obtained by means of the aliphatic diazo compounds in a manner analogous to that used to prepare the chloromethyl derivatives of arsenic [9]. It was thought to be of great interest to increase the amount of organic arsenic compounds synthesized by the diazomethane, to extend this method to other group V elements, as for example bismuth; the latter is reported below.

In contrast to diazomethane, diazoethane alkylates arsenic trichloride so readily that even if the ratio CH_3CHN_2: $AsCl_3$ = 1:1.5 moles, only the formation of the secondary arsine takes place and almost no α-chloroethyldichloroarsine is formed. This shows that the rate of the reaction of the alkylation of α-chloroethyldichloroarsine is considerably greater than the rate of the reaction of arsenic trichloride and diazoethane. In contrast, the formation of tri-(α-chloroethyl)-arsine, obtained by the reaction of diazoethane and arsenic trichloride (4:1), or by the reaction of an excess of diazoethane with di-(α-chloroethyl)-chloroarsine:

$$AsCl_3 + nCH_3CHN_2 \longrightarrow (CH_3CHCl)_3As + nN_2$$
$$(CH_3CHCl)_2AsCl + CH_3CHN_2 \longrightarrow (CH_3CHCl)_3As + N_2,$$

occurs only with difficulty, so that the secondary arsine is always isolated with the tertiary arsine from the reaction products.

Tri-(A-chloroethyl)-arsine, a colorless oil, is an unstable substance which decomposes on storage, as well as upon distillation in not too great a vacuum.

A substance which contains very little hydrolyzable chlorine and separates from the reaction mixture as an amorphous powder not prone to crystallization is obtained from the reaction of bismuth trichloride with diazomethane either in ether or in benzene, although all the solvents are dried with sodium. This compound, according to analysis, closely corresponds to the oxide of chloromethyl bismuth, and is characterized by the following specific behavior: spontaneous combustion of this product in the air, spontaneous carbonization throughout the whole mass when touched with a hot glass rod. Apparently, the formation of the oxide occurs according to the scheme:

$$BiCl_3 \xrightarrow[-N_2]{+CH_2N_2} ClCH_2BiCl_2 \xrightarrow[-2HCl]{+H_2O} ClCH_2BiO.$$

A readily hydrolyzed, unstable chloride, which is not prone to recrystallization, is obtained by treating the oxide with hydrochlofic acid and evaporating the solution in vacuum. According to analysis, the substance resembles in structure chloromethyl dichlorobismuth.

Therefore, the reaction of aliphatic diazo compounds with antimony, arsenic, and bismuth halides can be looked upon as a new general method for the synthesis of organic compounds of these elements.

EXPERIMENTAL

In all of the experimental work reported below, the usual method was used to prepare the solutions of the diazo compounds from the corresponding alkylnitrosourea by the decomposition of the latter with a solution of potassium hydroxide in the presence of a solvent (ether, and thiophene-free benzene). The diazo compound, so obtained, was dried and then the amount of the diazo compound in the solution was determined by means of benzoic acid.

1. Preparation of chloromethyldichlorostibine. 26.2 g of CH_2N_2 in 1100 ml of benzene, dried over solid potassium hydroxide (3 hours) and over sodium ribbon (0.5 hour), was added to 57 g of $SbCl_3$ in 75 ml of absolute benzene. The apparatus, which consisted of a three-necked flask with a mercury-sealed stirrer, a dropping funnel, and a gas take off tube (leading to the atmosphere through a Tishchenko bottle with sulfuric acid), was swept with nitrogen before the experiment, while the flask was heated. Continuing the passage of the nitrogen, a solution of $SbCl_3$ in benzene was added to the warm apparatus, the mixture was cooled to +3 − +5°, and the solution of diazomethane added over a 45 minute period. The reaction was accompanied by the evolution of heat (cooling) and nitrogen. The mixture was left over night at room temperature. A small amount of a residue, hydrolysis products, gathered at the bottom of the flask. For distillation of the benzene, the reaction flask was connected with a distillation flask (50 ml) by means of a tube placed in the reaction

flask located some distance above the precipitate. The benzene solution was sucked over into the distillation flask in parts (there was a clamp on the tube connecting the flasks), where the benzene was continually distilled in vacuum (60 mm) in a stream of dry, oxygen-free nitrogen. (The pump had a trap, cooled to minus 15-20°, in the line from the apparatus).

The residue, after the distillation of the benzene – a dark oil, was vacuum distilled on a free flame without a condenser, and the distillate collected in another distilling flask from which it was fractionally distilled. There was a decomposition at the end of the distillation. 33 g of an oil, which crystallized on cooling, came over at 120-125° at 25 mm. The residue in the flask, a dark, brittle tar, consisted of metallic antimony.

In this way, crude chloromethylchlorostibine was obtained by fractionation, as a dense, colorless oil, the main part of which came over at 96-99° at 4 mm. The pure chloromethylchlorostibine was a colorless crystalline substance; needles, m.p. 30-38° (in a closed capillary); b.p. 86.5° at 2 mm, 91-98° at 7 mm. d_{20}^{20} 2.677. The molten substance remained fluid at room temperature for a long time; it only crystallized when cooled below 0°. It was easily hydrolized by water to form a white precipitate of antimony oxides. A dark precipitate was formed on boiling with aqueous alkali (reduced antimony oxides).

0.1884 g substance: 22.98 ml 0.1 N $AgNO_3$. 0.2257 g substance: 27.49 ml 0.1 N $AgNO_3$. 0.2031 g substance: 14.15 ml 1/6 N $KBrO_3$. 0.2374 g substance: 19.50 ml 1/6 N $KBrO_3$. Found %: Cl 43.25, 43.19; Sb 50.70, 50.24. $ClCH_2SbCl_2$. Calculated %: Cl 43.93; Sb 50.29.

2. Preparation of tri-(chloromethyl)-stibine. 21.9 g (1 mole) of chloromethylchlorostibine, in 30 ml of absolute benzene, was placed in the apparatus described and 12.4 g (3 moles) of CH_2N_2 in 510 ml of benzene (dried with sodium ribbon) was added at 5-6° (cooling). Upon the addition of about 2/3 of the diazomethane, an intense evolution of heat and nitrogen occurred. The mixture was left over night. The benzene was distilled, as in Experiment 1, from a 25 ml distillation flask. The residue after the distillation of the benzene (19.0 g), was an oily, yellow colored liquid. The following fractions were obtained upon fractionation of the residue in a stream of nitrogen: 1) b.p. 86-101° at 3 mm – 2.8 g; 2) b.p. 102-104° at 3 mm – 4.1 g; 3) b.p. 104-106° at 3 mm – 4.5 g.

Upon redistillation of the third and second fractions, tri-(chloromethyl)-stibine, b.p. 105° at 3 mm, was obtained in the form of a dense colorless oil (8 g); d_{20}^{20} 2.038.

The substance could be stored under water for a long time (12-14 hours), but all of it completely hydrolyzed forming a white residue. It clouded rapidly on the surface in the air, apparently, as a result of oxidation; in a thin layer, (on a glass) it rapidly changed into a white solid product.

0.3820 g substance: 41.11 ml 0.1 N $AgNO_3$. 0.1721 g substance: 18.86 ml 0.1 N $AgNO_3$. 5.068 ml substance: 2.600 mg CO_2; 1.294 mg H_2O. 5.630 mg substance: 2.875 mg CO_2; 1.300 mg H_2O. 0.2944 mg substance: 21.44 ml 1/6 N $KBrO_3$. 0.1976 mg substance: 14.36 ml 1/6 N $KBrO_3$. Found %: Sb 44.36, 44.26; C 13.99, 13.93; H 2.85, 2.58; Cl 38.16, 38.86 $(ClCH_2)_3Sb$. Calculated %: Sb 43.19; C 13.68; H 2.22; Cl 39.4.

3. Preparation of tri-(chloromethyl)-dibromostibine. 1 g of tri-(chloromethyl)stibine was dissolved in 3 ml of dry, redistilled carbon tetrachloride, and 0.6 g bromine in 2 ml of CCl_4 was added to the solution with hand shaking. The solution was filtered and the solvent was vacuum distilled. The residue – a white powder – was recrystallized from benzene: white shiny needles, m.p. 90-90.5° (shrinks at 89-90°).

0.1008 g substance: 4.66 ml 0.1 N $AgNO_3$. 0.4379 g substance: 6.39 ml 0.1 N $AgNO_3$. Found %: Br 36.95, 37.04 $(ClCH_2)_3SbBr_2$. Calculated %: Br 37.42.

4. Reaction of diazomethane with antimony pentachloride. 50 g of $SbCl_5$ in 55 ml of absolute benzene was treated with 4 g of diazomethane in 220 ml of benzene at minus 14-20° and, at the end, at –4 to –3°. The benzene was vacuum distilled. The residue – a violet colored oily liquid (21.5 g), which crystallized on standing – contained 8 g of trivalent antimony in contrast to the 12.2 g of pentavelent antimony used in the reaction, according to the analysis. On redistillation the residue came over at 99-100° (8 mm) as a liquid, which crystallized in the receiver and possessed all of the properties of antimony trichloride.

If the residue after distillation of the benzene was treated with hydrochloric acid (with heating), and the insoluble part extracted with benzene and dried with Na_2SO_4, then after the distillation of the solvent, a small amount of an oil, b.p. 250-270° and characteristic odor of diphenylmethane was obtained.

5. Preparation of di-(α-chloroethyl)-chloroantimony. The apparatus and the procedure was the same as for Experiment 1. A solution of 17.2 g of (1 mole) $SbCl_3$ in 50 ml of benzene was cooled to 0° and a solution of 8.44 g (2 moles) of CH_2N_2 in 485 ml of benzene, dried for 3 hours over KOH sticks and then for 0.5 hours over sodium ribbon, was added to it with stirring.

At first, the reaction was affected at 2-3° and, at the end, at 5-6° (cooling with ice and salt). The addition of the diazoethane required 1 hour. The mixture was left overnight. The benzene was distilled as in Experiment 1 (30 ml distillation flask). The residue was a brownish red oil (18 g). On distillation in vacuum, 10.5 g of di-(α-chloroethyl)-chloroantimony came over at 83-90° at 3 mm; a slightly colored, dense liquid.

Pure di-(α-chloroethyl)-chloroantimony was a colorless oil, b.p. 88-88.5° at 3 mm, or 69.5° at 1 mm, d_{20}^{20} 1.831. It clouded up on contact with air as a result of oxidation; it did not seem to hydrolyze in water.

8.035 mg substance: 4.963 mg CO_2; 1.988 mg H_2O. 7.305 mg substance: 4.240 mg CO_2; 1.510 mg H_2O. 12.68 mg substance: 6.374 ml 0.02 N $AgNO_3$. 15.02 mg substance: 7.637 ml 0.02 N $AgNO_3$. 0.305 g substance: 21.33 ml 1/6 N $KBrO_3$. 0.2360 g substance: 16.55 ml 1/6 N $KBrO_3$. Found %: C 16.84, 16.57; H 2.76, 2.31; Cl 36.52, 36.06; Sb 42.63 , 42.90. $(CH_3CHCl)_2SbCl$. Calculated %: C 16.9; H 2.82; Cl 37.5; Sb 42.84.

Dichlorodiethylchloroantimony (1.6 g), when oxidized with 5 ml of peroxide in 5 ml of water, slowly (15-20 hours) changed (mixing) into a white powder of dichloroethylstibianic acid (1.3 g), which did not melt when heated to 190°.

0.1716 g substance: 12.5 ml 1/6 N $KBrO_3$. 0.2900 g substance: 20.9 ml 1/6 N $KBrO_3$. 13.59 g substance: 4.656 ml 0.02 N $AgNO_3$. 12.12 g substance: 4.17 ml 0.02 N $AgNO_3$. Found %: Sb 44.55, 44.08; Cl 24.30, 24.40. $(CH_3CHCl)_2SbO_2H$. Calculated %: Sb 43.30; Cl 25.24.

6. Preparation of di-(α-chloroethyl)-chloroarsine. A solution of 13.8 g of diazoethane (2.5 moles) in 500 ml of benzene, dried over KOH sticks for 3 hours, was added dropwise (about 1 hour) to a solution of 17 g (1 mole) of redistilled $AsCl_3$ in 50 ml of dry benzene. The reaction was effected at first at 0°, and, at the end, at 3-5° (cooling with ice and salt). The mixture was left over night and then the benzene was distilled off at 50-100 mm. The residue, a colored oil, was vacuum distilled, di-(α-chloroethyl)-chloroarsine, came over at 51-54° at 1 mm; yield 12 g (40% of theory on the diazoethane).

With a ratio of $AsCl_3$ to diazoethane of 1:1.5 moles, on distillation, the excess $AsCl_3$ first came over and then di-(α-chloroethyl)-chloroarsine, in a somewhat greater yield than above, distilled. When the amount of the diazoethane was greater than 2.5 moles to 1 mole of $AsCl_3$, some of the tertiary arsine was formed along with the secondary derivative. The preparation of the former is given below.

Di-(α-chloroethyl)-chloroarsine was a colorless oil, b.p. 51.5° at 1 mm, 61-61.5° at 3 mm, d_{20}^{20} 1.553, $n_D^{21.5}$ 1.5370. It darkened on standing.

3.850 mg substance: 2.835 mg CO_2; 1.035 mg H_2O. 4.920 mg substance: 8.700 mg CO_2; 1.885 mg H_2O. 11.71 mg substance: 7.369 ml 0.02 N $AgNO_3$. 12.82 mg substance: 8.07 ml 0.02 N $AgNO_3$. 0.1172 g substance: 9.8 ml 0.1 N I_2. 0.1528 g substance: 12.7 ml 0.1 N I_2. Found %: C 20.08, 20.51; H 3.79, 4.19; Cl 44.63, 44.65; As 31.71, 31.60. $(CH_3CHCl)_2AsCl$. Calculated %: C 20.23; H 3.37; Cl 44.88; As 31.49.

7. Preparation of tri-(α-chloroethyl)-arsine. 19 g of redistilled $AsCl_3$ (1 mole) was treated in the above manner with 23.2 g of diazoethane (4 moles) in 950 ml of benzene. The reaction mixture, containing an excess of diazoethane, was left in an ice bath overnight. The further processing was the same as Experiment 6. The residue was fractionated in vacuum and a fraction, b.p. 40-68° at 1 mm, 7.9 g; and a fraction b.p. 69.5-70.2° at 1 mm, 7.2 g, were obtained. The last fraction was pure tri-(α-chloroethyl)-arsine. On redistillation in a smaller vacuum, it decomposed considerably: b.p. 81-82° at 2 mm, 94-95° at 4 mm. Pure tri-(α-chloroethyl)-arsine was a colorless oil, d_{20}^{20} 1.445, n_D^{20} 1.5307; on storage under ordinary conditions, it slowly darkened; depending on the length of time stored it gave, in addition to tri-(α-chloroethyl)-arsine, a lower-boiling fraction and considerable tarry residue on distillation.

4.455 mg substance: 4.465 mg CO_2; 1.975 mg H_2O. 4.595 mg substance: 4.635 mg CO_2; 1.940 mg H_2O. 0.2283 g substance: 25.80 ml 0.1 N AgNO. 0.1391 g substance: 15.65 ml 0.1 N $AgNO_3$. 0.1656 g substance: 12.59 ml 0.1 N $Na_2S_2O_3$. 0.2123 g substance: 15.99 ml 0.1 N $Na_2S_2O_3$. Found %: C 27.40, 27.51; H 4.97, 4.72; Cl 40.07, 39.90; As 28.52, 28.25. $(CH_3CHCl)_3As$. Calculated %: C 27.17, H 4.53; Cl 40.0; As 28.26.

Di-(α-chloroethyl)-chloroarsine was obtained on the redistillation of the fraction, with b.p. 40-68° at 1 mm, and was identified by its boiling point, refractive index, and analysis for arsenic.

Tri-(α-chloroethane)-arsine can also be obtained by the action of diazoethane (1.5 mole) on di-(α-chloroethyl)-chloroarsine (1 mole) under the conditions given above. But under these conditions, the reaction products contained some unalkylated di-(α-chloroethyl)-chloroarsine along with the tri-α-chloroethyl)-arsine.

8. Reaction of diazomethane with bismuth trichloride. A solution of 5 g of $BiCl_3$ in 70 ml of absolute ether was prepared in a separate dish isolated from the air, and, while it was carefully protected from moisture, was added to the reaction flask under nitrogen. The reaction flask, fitted with a mercury-sealed stirrer, a dropping funnel, a thermometer, and a gas outlet tube, was dried carefully before the experiment by blowing dry nitrogen through while it was heated. 1.2 g of diazomethane in ether (70 ml) dried over sodium was added, dropwise with stirring and cooling (0-3°), in 40 minutes. With this, a violent evolution of nitrogen and the formation of a light yellow, almost colorless, precipitate occurred in the flask. The liquid was allowed to stand overnight at the temperature of melting ice. The precipitate was filtered by sucking over the reaction mixture, containing the suspended precipitate (mechanical stirrer) onto a hermetically sealed funnel by means of a vacuum. The precipitate and the funnel were placed in a vacuum desiccator. After removal of the ether, a light, silver green powder was obtained as the reaction product. Yield ~5 g. The substance dissolved in concentrated hydrochloric acid. When it was touched with a heated stick, a spontaneous carbonization occurred throughout the entire mass of the powder. •

4.00 mg substance: 0.785 mg CO_2; 0.540 mg H_2O. 3.375 mg substance: 0.605 mg CO_2; 0.795 mg H_2O. 0.1428 g substance: 0.1058 g Bi. 15.91 mg substance: 2.27 ml 0.02 N $AgNO_3$. 11.19 mg substance: 1.52 ml 0.2 N $AgNO_3$. Found %: C 5.35, 4.89; H 1.9, 2.63; Cl 9.63, 10.12; Bi 74.0. CH_3ClBiO. Calculated %: C 4.42; H 0.73; Cl 13.0; Bi 76.2.

1.5 g of the substance, whose analysis is given above, was dissolved in 3 ml of concentrated hydrochloric acid and the solution was evaporated in vacuum (2-3 mm) at 40°. The residue was a light yellow syrupy mass which crystallized after some time.

7.705 mg substance: 1.165 mg CO_2; 1.30 mg H_2O. 7.925 mg substance: 1.255 mg CO_2; 1.405 mg H_2O. 0.1217 g substance: 0.0687 g Bi. 0.1161 g substance: 10.31 ml 0.1 N $AgNO_3$. Found %: C 4.12, 4.31; H 1.89, 2.05; Bi 56.7; Cl 31.48. $CH_2ClBiCl_2$. Calculated %: C 3.65; H 0.608; Bi 63.47; Cl 32.42.

The substance obtained decomposed during the purification. When it was dissolved in absolute solvents prepared in the usual manner, a precipitate, apparently oxides, formed.

SUMMARY

1. It was shown that the diazo method for the synthesis of aliphatic organo-elemental compounds can be applied for the preparation of organo-antimony, arsenic, and bismuth compounds.

2. Chloromethyldichlorostibine and tri-(chloromethyl)-stibine were obtained by the reaction of antimony trichloride with diazomethane; and di(α-chloroethyl)stibine with diazoethane. Antimony pentachloride reacted with a molar quantity of diazomethane to form antimony trichloride.

3. Di-(α-chloroethyl)-chloroarsine and tri-(α-chloroethyl)-arsine could be obtained by the reaction of arsenic trichloride with diazoethane. The latter substance was an unstable compound, which decomposed when stored under ordinary conditions.

4. Bismuth trichloride and diazomethane formed the unstable oxide of chloromethyl bismuth, which, on treatment with hydrochloric acid, gave the unstable chloromethyldichlorobismuth.

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SYNTHESIS OF ALIPHATIC ORGANO-ELEMENTAL COMPOUNDS BY THE DIAZO METHOD

II. SYNTHESIS OF COMPOUNDS OF THE GROUP V ELEMENTS – ORGANO-PHOSPHORUS COMPOUNDS

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In the previous communication [1], it was shown that aliphatic diazo compounds can be used for the synthesis of organo-antimony, arsenic, and bismuth compounds. In order to increase the scope of this reaction, the synthesis of organophosphorus compounds by the diazo method was studied; with the expectation of producing the difficultly accessible, and little investigated halodialkylphosphine compounds.

In 1947 Plets [2] reported that the reaction of diazomethane with phosphorus trichloride leads to the formation of tarlike products from which no homogeneous compound could be isolated. Previously, Staudinger also could not observe any organophosphorus compound formation upon the reaction of PCl_3 with diazomethane [3]. Therefore, in contrast to the aromatic diazo compounds [4], the aliphatic had not been used up to now for the preparation of organophosphorus compounds. However, it was shown by the authors that under favorable conditions,(low temperatures) aliphatic diazo compounds could be used successfully for the preparation of α-halodialkylphosphine compounds. In principle this reaction differs little from the previously studied reaction of the aliphatic diazo compounds with the halides of other elements.

At room temperature, diazomethane and diazoethane react very violently with phosphorus trichloride (in ether solution) to form nitrogen and a tarlike precipitate, which liquifies in the air. However, when the reaction temperature is decreased to minus 60-50°, the amount of precipitate is greatly decreased, and chloromethyldichlorophosphine and α-chloroethyldichlorophosphine (respectively) are obtained as the main reaction products in 40% yields calculated on the diazo compound.

$$PCl_3 \xrightarrow{CH_2N_2} ClCH_2PCl_2 + N_2$$

$$PCl_3 \xrightarrow{CH_3CHN_2} CH_3CHClPCl_2 + N_2$$

Small amount of esters of dichlorophosphoric acid (CH_3OPCl_2 and $C_2H_5OPCl_2$ respectively) are obtained as side products, as a result of the alkylation of dichlorophosphoric acid due to the partial hydrolysis of PCl_3 with traces of water introduced with the solvents.

$$PCl_3 + H_2O \longrightarrow HOPCl_2 + HCl; \qquad RCHN_2 + HOPCl_2 \longrightarrow RCH_2OPCl_2 + N_2.$$

On the reaction of phosphorus trichloride with diazobutane, α-chloro-n-butyldichlorophosphine is formed (in addition to the side product, butyl dichlorophosphite) which, in further processing is transformed into the acid chloride of α-chloro-n-butylphosphinic acid, which was isolated from the reaction products.

The ease of oxidation of the alkyldichlorophosphines to form derivatives of P^V was also observed for α-chloroethyldichlorophosphine (cotton soaked with $CH_3CHClPCl_2$ flamed spontaneously in the air), while chloromethyl- and bromomethyldihalophosphines are relatively stable in the air.

Phosphorus tribromide reacts analogously with diazomethane to give 50% yield of bromomethyldibromophosphine. A series of its derivatives was also prepared (see the experimental section). It is interesting that chloromethyl phosphorus tetrachloride is readily chlorinated to CCl_3PCl_4, which forms the stable polychloroacid chloride $CCl_3PO(Cl)OH$, m.p. 79°, on hydrolysis with water. Trichloromethylphosphinic acid can be obtained by the hydrolysis of the above acid, as well as from diethyl trichloromethylphosphinate; reported by Kamay [5], with hydrochloric acid (in a sealed ampoule); m.p. 87-89°.

The reaction of α-chloroalkyldichlorophosphines with aliphatic diazo compounds does not lead to the formation of di- and trichloroalkylphosphines; the reaction, instead, results in more complex solid products. Analogous compounds are obtained as side products from the reaction of aliphatic diazo compounds with PCl_3 and PBr_3.

Therefore, the above reaction can be used as a convenient method for the synthesis of the difficultly accessible primary alkylhalophosphines. However, di- and trialkyl-substituted derivatives of phosphorus, as well as the mono- can be prepared with the aid of aliphatic diazo compounds, if the phosphorus pentahalides are used. These reactions were studied with diazomethane and diazoethane, and phosphorus pentachloride. It appears that the course of this reaction was effected by the lower solubility of PCl_5 in organic solvents, as compared with the solubility of the alkyl substituted derivatives of PCl_5($RPCl_4$, R_2PCl_3, etc.), and by the greater rate of alkylation of the latter, when compared to PCl_5.

The reaction, for example, of diazomethane with phosphorus pentachloride, apparently, proceeds under the conditions of "excess" diazo-compound and does not stop at the monoalkylated stage, but goes on to the trialkylated, so that the oxide of tri-(chloromethyl)-phosphine forms in a 50-70% yield according to the equation:

$$PCl_5 + 3CH_2N_2 \longrightarrow (ClCH_2)_3PCl_2 \xrightarrow[\text{or } SO_2]{\text{moisture}} (ClCH_2)_3PO.$$

The reaction between diazoethane and phosphorus is more complex; the acid chloride of di-(α-chloroethyl)-phosphinic acid, which gave di-(α-chloroethyl)-phosphinic acid on hydrolysis, was isolated from the reaction products.

It is interesting that phosphorus oxychloride and oxybromide, in contrast to phosphorus pentachloride, could not be alkylated with diazomethane or diazoethane even on the artificial decomposition of the diazo compounds with catalysts (Cu, $CuSO_4$). The only product of the reaction, for example with $POCl_3$, along with the recovered phosphorus oxychloride, was the ester of dichlorophosphoric acid formed in small quantities as a result of the partial hydrolysis of phosphorus oxychloride followed by the alkylation of the dichlorophosphoric acid with the diazo compound.

$$POCl_3 \xrightarrow{H_2O} HOPOCl_2 \xrightarrow{CH_2N_2} CH_3OPOCl_2.$$

EXPERIMENTAL

1. Chloromethyldichlorophosphine, $ClCH_2PCl_2$. An ether solution (1 mole) of diazomethane (25 g of CH_2N_2 in 750 ml ether), dried by a three hour cooling to −70° over solid potassium hydroxide, was added with efficient mechanical stirring to a solution of 200 g of PCl_3 (2.5 mole) in 200 ml of dry ether cooled to −70°. The temperature of the reaction mixture was kept at minus 55-65°. An energetic reaction occurred, accompanied by the evolution of nitrogen (about 14 liters of gas) and the formation of a white precipitate. The mixture was then allowed to stand overnight, slowly warming up to room temperature; then the reaction products of five experiments were combined and processed together. The precipitate was filtered onto a glass filter protected from moisture, and washed many times with dry ether; it was dried in a vacuum desiccator, over P_2O_5 and solid alkali to remove the ether. A total of 32 g of dry residue, which hydrolyzed in the air, was obtained.

The residue – organophosphorus compounds – was soluble in water, alcohols, ketones, and insoluble in benzene and chloroform. The substance was decomposed on recrystallization.

The ether of the filtrate was distilled through a column and the residue fractionated through the column, first at ordinary pressure and then at 140 mm. Besides PCl_3, the following fractions were collected (uncorrected b.p.'s): I) 42-47.5° −13 g; II) 47-62° at 140 mm, −54 g; III) 62-76° at 140 mm −7 g; IV) 77-78° at 140 mm −175 g.

Fraction I was redistilled at ordinary pressure: a) 84-90° −3.0 g; b) 91-92° −4.8 g; c) 92-93.5°−3 g.. Fraction Ib had b.p. 91-92° (uncorrected); or 94-95° (corrected).

d_{20}^{20} 1.3995; n_D^{20} 1.4750.

Found %: Cl 52.91, 53.10. CH_3OPCl_2. Calculated %: Cl 53.38.

Therefore, fraction Ib was methyl dichlorophosphate described by Kovalevsky [7]; b.p. 95-96°; d_4^{20} 1.3980; n_D^{20} 1.47725.

Fraction II was redistilled at ordinary pressure d) 102.3-105° (uncorrected) −16.2 g; e) 105-107° (uncorrected) −31.3 g; f) a small amount of a higher boiling fraction. Fraction IIe had b.p. 105-107.6° (uncorrected) or 108-110° (corrected; the substance did not contain P^{III}).

Found %: Cl 68.38, 69.36. $POCl_3$. Calculated %: Cl 69.38. Therefore Fraction IIe was phosphorus oxychloride*.

Fraction IV, b.p. 77-78° (uncorrected) or 80-81° (corrected); d_{20}^{20} 1.5289, n_D^{20} 1.5247 – was a dense, transparent, colorless liquid with a sharp, unpleasant odor. The substance clouded in the air as a result of hydrolysis.

2.860 mg, 5.410 mg substance: 0.845 mg, 1.0670 mg CO_2; 0.475 mg, 0.800 mg H_2O. 9.905 mg, 12.160 mg substance: 9.719 ml, 12.160 ml 0.02 N $AgNO_3$. 0.2045 g, 0.2542 g substance in 25 ml 0.5 N KOH: 27.30 ml, 27.4 ml 0.1 N $AgNO_3$. 0.3136 g, 0.3304 g substance: 0.3955 g, 0.4155 g molybdate. 0.3945 g substance; 16 g benzene: Δt 0.830°. Found %: C 8.05, 7.31; H 1.46, 1.46; total Cl 69.59, 69.43; hydrolyzable Cl 47.31, 47.08; P 20.85, 20.81; M 152. $ClCH_2PCl_2$. Calculated %: C 7.90; H 1.32; total Cl 70.25; hydrolyzable Cl 46.84; P 20.45; M 151.5.

Therefore Fraction IV was chloromethyldichlorophosphine (yield 40% of the theoretical on the diazomethane).

2. Phosphorus chloromethyltetrachloride, $ClCH_2PCl_4$. 2.5 g of chlorine (1 mole) in 10 ml of CCl_4 was added at 0 to +5° to a solution of 5 g (1 mole) of chloromethyldichlorophosphine in 5 ml CCl_4. A white crystalline precipitate formed rapidly, while the color of the chlorine disappeared. Then about 80% of the solvent was vacuum distilled at not over 30-35° (in the bath). The residue (5.5 g) was filtered and washed with cold CCl_4 (all of the operations were performed in the absence of moisture). The white crystals fumed in the atmosphere and liquified; m.p. 102-104° (decomp.) in a closed capillary.

A partial decomposition of the substance occurred on recrystallization.

0.1090 g substance in 25 ml 0.5 N KOH in the cold: 19.85 ml 0.1 N $AgNO_3$. Found %: hydrolyzable Cl 64.64. $ClCH_2Cl_4$. Calculated %: hydrolyzable Cl 64.39.

3. The di-acid chloride of chloromethyl phosphinic acid, $ClCH_2POCl_2$. a) The oxidation of chloromethylchlorophosphine with nitrogen dioxide. 10 g of chloromethylchlorophosphine, in 10 ml of dry CCl_4, was oxidized at −5 to 0° with dry nitrogen dioxide, which was slowly passed into the reaction mixture (3.7 g of NO_2 in 30 min). The nitrogen dioxide was added as rapidly as it was decolorized. Oxidation stopped just as soon as a permanent red color formed, due to the formation of tarry products. The reaction mixture was then swept with dry air and immediately vacuum distilled. 7 g (yield 60% of the theoretical) of the di-acid chloride of chloromethylphosphinic acid, b.p. 103° at 30 mm, was obtained; it was a colorless, dense liquid, with a characteristic acid chloride odor.

d_{20}^{20} 1.6444; n_D^{20} 1.4945.

11.800 mg substance: 10.55 ml 0.02 N $AgNO_3$. 0.1410 g substance in 25 ml 0.5 N KOH: 16.9 ml 0.1 N $AgNO_3$. 0.2756 g substance; 16 g benzene: Δt 0.515°.

Found %: total Cl 63.48; Hydrolyzable Cl 42.54; M 171. CH_2OCl_3P. Calculated %: Total Cl 63.58; Hydrolyzable Cl 42.38; M 167.5.

b) The treatment of phosphorus chloromethyltetrachloride with sulfur dioxide. Phosphorus chloromethyltetrachloride, obtained in the above way from 10 g of chloromethyldichlorophosphine, was treated in the cold (without any preliminary distillation of the solvent) with dry sulfur dioxide until the precipitate dissolved, and subsequently for 15 minutes. The CCl_4 is removed in vacuum at 30-35° (in a bath) and the residue fractionated. 8.5 g of a liquid which was $ClCH_2POCl_2$, b.p. 102-103° at 30 mm or 63° at 2 mm, was obtained. Yield about 80% of the theoretical.

Found %: Hydrolyzable Cl 42.03. $ClCH_2POCl_2$. Calculated %: Hydrolyzable Cl 42.38.

4. Chloromethylphosphinic acid, $ClCH_2PO(OH)_2$. 2 g of the diacid chloride of chloromethylphosphinic acid was added, in parts, to 10 ml of water; it dissolved with the evolution of heat. After standing in a vacuum desiccator over P_2O_5 for one week, it crystallized. The wet crystals of the chloromethyl phosphinic acid were pressed on a plate and recrystallized from a mixture of benzene and nitromethane: thin long needles, m.p. 92°. Yield – quantitative.

* Careful distillation of the initial PCl_3 in the same column (20 theoretical plates) resulted in the isolation of the corresponding quantity of $POCl_3$. Therefore, the oxychloride was introduced as an impurity in the phosphorus trichloride.

5.862 mg, 4.230 mg substance: 2.010 mg, 1.428 mg CO_2; 1.715 mg, 1.428 mg H_2O. 15.10 mg, 15.11 mg substance: 5.630 ml, 5.700 ml 0.02 N $AgNO_3$. Found %: C 9.35, 9.21; H 3.27, 3.25; Cl 26.47, 26.80. Calculated %: C 9.19; H 3.07; Cl 27.20.

The substance was hygroscopic; the silver salt dissolved readily in water. Methyl chloride was not formed on heating with alkali.

5. Aniline salt of chloromethylphosphinic acid, $ClCH_2PO(OH)_2 \cdot C_6H_5NH_2$. 0.5 g of the acid was mixed with benzene with an excess of aniline (2 ml). After standing for two days, the precipitate was filtered and recrystallized from alcohol. Thin needles, m.p. 183°, (with decomp.) Yield – quantitative.

4.790 mg, 3.950 mg substance: 0.3008 ml, 0.2450 ml N_2 (20°, 752 mm) 0.1337 g substance: 12.0 ml 0.1 N KOH (phenolphthalein). Found %: N 7.17, 7.08; equiv. 111. Calculated %: N 6.26; equiv. 111.7.

6. Ethyl ester of chloromethylphosphinic acid, $ClCH_2PO(OC_2H_5)_2$. An alcoholic solution of sodium ethylate (2.8 g of sodium in 55 ml of absolute alcohol) was added to 8.3 g of the di-acid chloride of chloromethylphosphinic acid in 10 ml of ether at 0-5° until neutral to Congo. After filtration of the sodium chloride precipitate and distillation of the alcohol and the ether, the residue was fractionated in vacuum. Ethyl chloromethylphosphinate was a colorless liquid with a fruity odor; b.p. 86-87° at 2.5 mm.

d_{20}^{20} 1.1909; n_D^{20} 1.4360.

4.185 mg, 3.985 mg substance: 4.840 mg, 4.610 mg CO_2; 2.305 mg, 2.205 mg H_2O. 12.380 mg substance: 18.84 ml 0.02 N $AgNO_3$. 0.2552 g substance; 16 g benzene: Δt 0.435°. Found %: C 31.54, 31.55; H 6.16, 6.19; Cl 18.84; M 187.5. $ClCH_2PO(OC_2H_5)_2$. Calculated %: C 31.17; H 6.43; Cl 19.03; M 186.5.

7. α-Chloroethyldichlorophosphine, $CH_3CHClPCl_2$. 30 g of diazoethane (1 mole) in 800 ml of dry ether, dried in the usual manner, was added dropwise to 190 g of PCl_3 (2.5 mole) in 200 ml of dry ether cooled to –70°. The reaction was run at minus 55-60° in a nitrogen atmosphere; a considerable amount of heat evolved and a clouding of the solution occurred (white precipitate). The mixture was allowed to come to room temperature overnight and the precipitate dissolved completely. The ether was removed from the reaction products of 4 experiments (through a column) and the residue was distilled through a column. In addition to PCl_3 the following fractions were collected: I) to 44° (100 mm) –5 g; II) 40-46° (100 mm) –52 g; III) 46.5-50.9° (100 mm) –7 g; IV) 51.0 –52° (100 mm) –22 g; V) 53-61° (50 mm) –6 g; VI) 61.5-62.5° (50 mm) –100 g; VII) higher boiling residue – to 70° (7 mm) –10 g.

Fraction II was redistilled at ordinary pressure. The bulk of it distilled at 107-109° (corrected). The fraction did not contain trivalent phosphorus.

Found %: Cl 68.3, 69.1. $POCl_3$. Calculated %: Cl 69.38.

Therefore, Fraction II was phosphorus oxychloride (see Experiment 1).

The substance in Fraction IV, b.p. 51.0-52° at 100 mm and 117-118° (with decomp.) at ordinary pressure:

d_{20}^{20} 1.3300; n_D^{20} 1.4640.

Found %: total Cl 51.30, 51.80; hydrolyzable Cl 50.85, 51.48. P total 20.76; P^{III} 19.80; M 157, 150. $C_2H_5OPCl_2$. Calculated %: Cl hydrolyzable 48.30; P^{III} 21.1; M 147.

Therefore, Fraction IV was impure ethyl dichlorophosphate. Literature data [7]: b.p. 117-118°, d^0 1.316, n_D^{22} 1.7776.

For identification, the preparation was treated with a mixture of alcohol and diethylaniline. 5.3 g of Fraction IV was added to 15 g of diethylaniline, 5 g of absolute alcohol, and 50 ml of ether with cooling; the mixture was left over night. Diethylaniline hydrochloride (12 g) was filtered off and the filtrate was twice distilled in vacuum. 7 g of triethyl phosphate, b.p. 49° at 12 mm and n_D^{20} 1.4130 was obtained; this corresponded to the results given in the literature.

Fraction VI, b.p. 61.5-62.5° (uncorrected) at 50 mm or 63.5-64.5° (corrected) at 50 mm, was a colorless substance which fumed in the air. Cotton soaked with this substance flamed in the air.

d_{20}^{20} 1.4232; n_D^{20} 1.5090.

5.290 mg substance: 2.720 mg CO_2; 1.215 mg H_2O; 11.52 mg substance: 10.53 ml 0.02 N $AgNO_3$. 0.1870 g substance; 16 g benzene. Δt 0.355°. 0.1857 g, 0.1470 g substance. In 25 ml water (it hydrolyzed within 25 min). 22.50 ml 17.8 ml 0.1 N $AgNO_3$. Found %: C 14.10; H 2.55; Hydrolyzable Cl

43.02, 42.97; Total Cl 64.81; M 167.5. $CH_3CHClPCl_2$. Calculated %: C 14.51; H 2.41; Hydrolyzable Cl 42.90; Total Cl 64.35; M 165.5.

Therefore, Fraction VI was α-chloroethyldichlorophosphine (yield 35 % of theoretical based on the diazoethane).

8. Phosphorus α-chloroethyltetrachloride – $CH_3CHClPCl_4$. 5 g of α-chloroethyldichlorophosphine in 5 ml of CCl_4 was chlorinated at -5 to 0° with the calculated amount of chlorine in CCl_4. A white precipitate formed which, after removal of the main part of solvent, was filtered and washed with cold CCl_4. Fine, hygroscopic crystals were obtained.

0.1237 g substance. saponified in 25 ml 0.5 N. KOH, 20.75 ml 0.1 N. $AgNO_3$. Found %: hydrolyzable Cl 59.55. $CH_3CHClPCl_4$. Calculated %: hydrolyzable Cl 60.04.

9. Di-acid chloride of α-chloroethylphosphinic acid – $CH_3CHClPOCl_2$. A solution of 7.5 g of chlorine (1.05 mole) in 50 ml of CCl_4 was added dropwise, with cooling with ice and salt, to a solution of 16.5 g of $CH_3CHClPCl_2$ in 15 ml of CCl_4. The precipitated tetrachloride was treated, without separation, with a stream of SO_3 until it dissolved and then for 10 minutes more. Then the solvent was removed (half at ordinary pressure and the rest in vacuum). The residue was distilled; everything distilled at 70° at 8 mm. Yield – 90-95 % of theory. It was a colorless liquid with a characteristic acid chloride odor.

d_{20}^{20} 1.5424; n_D^{20} 1.4930.

0.1423 g substance. saponified in 25 ml 0.5 N. KOH; 15.5 ml 0.1 N. $AgNO_3$. 11.30 mg, 11.50 mg substance: 9.396 ml, 9.609 ml 0.02 N. $AgNO_3$. 4.974 mg, 4.894 mg substance: 2.428 mg, 2.372 mg CO_2; 1.199 mg, 1.1210 mg H_2O. 0.2174 g substance; 16 g benzene: Δt 0.393°. Found %: C 13.34, 13.31; H 2.70, 2.70; hydrolyzable Cl 38.62; Total Cl 58.94, 59.26; M 178; $CH_3CHClPOCl_2$. Calculated %: C 13.23; H 2.20; hydrolyzable Cl 39.10; Total Cl 58.68. M 181.5.

10. α-Chloroethylphosphinic acid – $CH_3CHClPO(OH)_2$. 2g of $CH_3CHClPOCl_2$ was hydrolyzed with 3 ml of water. The excess water was removed in a desiccator over P_2O_5. The crystalline mixture was pressed on a plate, and the crystals recrystallized from a mixture of benzene and nitromethane.

Colorless needles; M.p. 99-100°. Yield – quantitative.

3.494 mg, 4.395 mg substance: 2.205 mg, 2.750 mg CO_2; 1.297 mg, 1.507 mg H_2O. 10.70 mg, 14.20 mg substance: 3.73 ml, 4.98 ml 0.02 N $AgNO_3$. Found %: C 17.21, 17.07; H 4.15, 3.83; Cl 24.75, 24.90. $CH_3CClPO(OH)_2$. Calculated %: C 16.61; H 4.25; Cl 24.57.
The silver salt was readily soluble in water.

11. Anilide of α-chloroethylphosphinic acid – $CH_3CHClPO(NHC_6H_5)_2$. An excess of aniline (5 g) was added to 2 g of the diacid chloride in benzene. After 24 hours the aniline hydrochloride was filtered off; it was washed with acidified water to remove the excess aniline, and the benzene was removed in vacuum from the dried solution. The noncrystalline oil was dissolved in alcohol; the addition of water precipitated white crystals. The m.p. was 154-155° after recrystallization from aqueous alcohol.

11.50 mg; 10.98 mg substance: 4.00 ml, 3.74 ml 0.02 N. $AgNO_3$. 3.300 mg, 4.930 mg substance: 0.30184 ml, 0.45864 ml N_2 (27°, 745 mm). Found %: Cl 12.33, 12.20; N 10.15, 10.35. $CH_3CHClPO(NHC_6H_5)_2$. Calculated %: Cl 12.05, N 9.56.

12. Ethyl ester of α-chloroethylphosphinic acid – $CH_3CHClPO(OC_2H_5)_2$. 50 ml of dry ether, 3 g of absolute alcohol and 9 g of diethylaniline were placed in a flask. A solution of 5.4 g of the di-acid chloride of α-chloroethylphosphinic acid in 10 ml of ether was added, dropwise in the cold (ice and salt). After 24 hours the diethylaniline hydrochloride was filtered; the excess diethylaniline was removed with acidified water, the ether layer dried, and the ether removed.

On distillation, a fraction, b.p. 93° at 5 mm or 96° at 7 mm, was collected. The yield of the ester – 3.5 g. It was a colorless liquid with a pleasant fruity odor.

d_{20}^{20} 1.1474; n_D^{20} 1.4370.

17.200 mg, 26.010 mg substance: 4.25 ml, 6.50 ml 0.02 N. $AgNO_3$. 0.2177 g substance; 16 g benzene: Δt 0.360°. Found %: Cl 17.54, 17.74; M 193. $CH_3CHClPO(OC_2H_5)_2$. Calculated %: Cl 17.71; M 200.5.

13. Reaction of diazobutane with phosphorus trichloride. a) Preparation of nitrosobutylurea. Hydrochloric acid was added dropwise with cooling to -5to 0° to a solution of 100 g of butylamine in 300 ml of water until an acidic reaction to methyl red was obtained. 400 g of water and 250 g of urea were added to the solution, and it was refluxed for three hours. After cooling, 120 g of sodium nitrite in 300 g of water was added to the reaction mixture (the main part of the crystals of the butyl urea dissolved), and the mixture slowly added to a mixture of 95 g of sulfonic acid and 600 g of finely chopped ice with energetic stirring and cooling to -5 to +5°.

The nitroso butylurea separated as a light foam, which was filtered on a glass filter, washed with a small amount of water, and dried in a desiccator. It was stored at temperatures below 10°.

b) Preparation of diazobutane. 100 g of nitrosobutylurea, was added, in portions with shaking and cooling to -5 – 0°, to a mixture of 500 ml of urea and 200 ml 70% aqueous solution of KOH. The ether layer was slowly colored red-orange. In order to prevent the decomposition of the nitrosomethyl urea, the ether layer containing the diazobutane was decanted. The yield was 25 g of diazobutane (analyzed with benzoic acid).

c) Preparation of the acid chloride of α-chlorobutylphosphinic acid – $CH_3(CH_2)_2CHClPOCl_2$. 22 g of diazobutane (1 mole) in 450 ml of ether, dried in the usual manner by cooling over KOH, was added dropwise with cooling, by means of CO_2 and acetone, to a solution of 70 g (2 moles) of PCl_3 in 100 ml of dry ether. The reaction occurred rapidly. After addition of the diazo compound, the ether was distilled through a column, and the residue fractionated. The following fractions were collected: I) b.p. 63-64.5° at 30 mm – 7 g, II) b.p. 84° at 25 mm – 10.5 g.

Fraction I boiled, at ordinary pressure, at 155-157° with decomposition.

d_4^{20} 1.1661.

Found %: Hydrolyzable Cl 40.0; Total Cl 39.4; P^{III} 17.7; M 180. $C_4H_9OPCl_2$. Calculated %: Hydrolyzable Cl 40.5; Total Cl 40.5; P^{III} 17.7; M 175.

Therefore, Fraction I was the acid chloride of butylphosphoric acid, whose constants were reported by Kovalevsky [7]: b.p. 157°, d_4^{20} 1.1657.

Fraction II, b.p. 84° at 25 mm, was a colorless liquid with a sharp acid chloride odor. The product did not contain P^{III}.

d_{20}^{20} 1.3236; n_D^{20} 1.5010.

0.1067 g, 0.1080 g substance in 25 ml 0.5 N KOH: 10.30 ml, 10.60 ml 0.1 N $AgNO_3$. 10.605 mg substance: 7.585 ml 0.02 N $AgNO_3$. 0.2300 g substance: 16 g benzene: Δt 0.330°. Found %: Hydrolyzable Cl 34.9; Total Cl 50.75; M 212. Calculated %: hydrolyzable Cl 33.89; Total Cl 50.84; M 209.5.

Therefore, this fraction was the acid chloride of α-chlorobutylphosphinic acid.

14. Reaction of diazomethane and PBr_3. Bromomethyldibromophosphine – $BrCH_2PBr_2$. A solution of 2.72 g of diazomethane (1 mole) in 150 ml of ether, dried in the usual manner by cooling over solid KOH and then for 2 hours over sodium ribbon, was added, slowly, with stirring at a temperature of minus 50-55°, to a solution of 52.7 g (3 moles) of PBr_3 in 50 ml of ether.

The diazomethane decomposed as it was added, and a colorless amorphous precipitate formed. The reaction mixture was then warmed to room temperature, the precipitate filtered, the ether distilled through a column, and the residue fractionated. After a careful distillation, in addition to the excess of PBr_3, there was isolated a 9.5 g fraction with b.p. 70° at 4 mm and $d_{4^\circ}^{20}$ 2.6357.

5.995 mg, 3.825 mg substance: 1.212 mg, 0.775 mg CO_2; 0.775 mg, 0.411 mg H_2O. 14.4 mg, 17.97 mg substance: 7.362 ml, 9.386 ml 0.02 N $AgNO_3$. 0.2838 g, 0.2880 g substance: 20.72 ml, 19.02 ml 0.1 N $AgNO_3$. 0.1894 g, 0.1810 g substance: 0.2363 g, 0.1987 g molybdate. Found %: C 5.51, 5.52; H 1.14, 1.20; Total Br 83.20, 83.47; hydrolyzable Br 58.34, 58.91; P 9.20, 10.95; $BrCH_2PBr_2$. Calculated %: C 4.22; H 0.70; total Br 84.40; hydrolyzable Br 56.25; P 10.85.

Bromomethyldibromophosphine was obtained in a 50% yield based on the diazomethane. When the ratio $PBr_3:CH_2N_2 = 2:1$ and $PBr_3:CH_2N_2 = 1:1$, the amount of the precipitate increased sharply and the yield of the $BrCH_2PBr_2$ dropped until, in the latter case, it was only 15-20%. The residue was readily hydrolyzed in the air with the formation of bromine; it was soluble in water and in alcohols, and insoluble in benzene, carbon tetrachloride, and chloroform. It decomposed on recrystallization. The substance was an organophosphorus compound.

15. Oxidation of bromoethyldibromophosphine with nitrogen dioxide. The acid bromide of bromomethylphosphinic acid, $BrCH_2POBr_2$. 4.9 g of dry NO_2 was passed, over a period of 25 min at 5-10°, into a solution of 17 g of $BrCH_2POBr_2$ in 50 ml of dry CCl_4. At the start of the passage of the gas, a precipitate formed which dissolved at the end of the reaction, whereupon the temperature of the reaction mixture began to rise. After standing for a half hour at room temperature, the nitrogen dioxide and the solvent were removed in vacuum and the residue fractionated. Weight of the product – 10.8 g; it distilled at 118-120° at 7 mm or 112-113° at 2 mm. It was a solid substance, m.p. 38°, which readily supercooled. The constants of the supercooled substance were: d_4^{20} 2.7030, n_D^{20} 1.5120. Yield – 60% of the theoretical based on the phosphine.

0.2972 g, 0.2075 g substance: 19.91 ml. 13.85 ml 0.1 N. $AgNO_3$. 0.6510 g substance; 16 g benzene; Δt 0.6650. Found %: hydrolyzable Br 53.53, 53.34; M 315.0. $BrCH_2POBr_2$. Calculated %: hydrolyzable Br 53.15; M 300.5. Bromomethyldibromophosphine reacted energetically with metallic mercury to form a compound which could not be vacuum distilled.

16. Diethyl ester of bromomethylphosphinic acid – $BrCH_2PO(OC_2H_5)_2$. A mixture consisting of 20 ml of ether and 3.4 g of absolute alcohol was added, dropwise in the cold (ice and salt), to 10.8 g of the acid bromide, $BrCH_2POBr_2$, in 40 ml of dry ether followed by a solution of 10.3 g of diethylaniline in 50 ml of ether; the reaction mixture was allowed to stand over night at room temperature.

The precipitate of diethylaniline hydrobromide was filtered and carefully washed with ether. After distillation of the ether from the filtrate, the residue was fractionated. The diethyl ester of bromomethylphosphinic acid, b.p. 99° at 1 mm, was obtained in a yield of 50% based on the weight of the acid bromide.

d_4^{20} 1.4474; n_D^{20} 1.4585.

0.1620 g substance: 1.36 ml 0.1 N. $AgNO_3$. 0.433 mg, 0.391 mg substance; 21.99 ml 20.00 ml 0.1 N. $Na_2S_2O_3$. Found %: Br 33.62; OC_2H_5 37.79, 38.15. $BrCH_2PO(OC_2H_5)_2$. Calculated %: Br 34.59; OC_2H_5 38.93.

17. Bromomethylphosphinic acid – $BrCH_2PO(OH)_2$. 2g of $BrCH_2POBr_2$ was hydrolyzed by means of 3 ml of water. The excess water was removed in a vacuum desiccator over P_2O_5. The acid was very hygroscopic, and it was very difficult to identify it; for this reason, it was transformed into the aniline salt by addition of an excess of aniline to a solution of the acid in benzene. Upon recrystallization of the salt from alcohol containing 1% aniline, thin needles, m.p. 187° (with decomp.) were obtained. The yield was theoretical.

4.403 mg, 4.495 mg substance: 0.2087 ml, 0.1960 ml N_2 (32°, 747 mm). 0.0809 g substance: 5.90 ml 0.1 N. KOH (phenolphthalein).

Found %: N 5.19, 4.90; equiv. 137. $BrCH_2PO(OH)_2 \cdot C_6H_5NH_2$. Calculated %: N 5.22; equiv. 134.

18. Reaction of diazomethane and diazoethane with phosphorus oxychloride. An ether solution of 13-14 g of dry diazomethane* in 400 ml of ether was added stepwise to 120 g of $POCl_3$ diluted with 50 ml of ether at -25 to -30° in the presence of dry copper sulfate (at first 1 g was added, and then 0.5 g was added twice during the course of the experiment. After the formation of the nitrogen stopped, the reaction mixture was allowed to come to room temperature, the ether was distilled through the column, and the residues from three such experiments were combined and distilled. After removal of the $POCl_3$ and a careful distillation of the residues, 6 g of a fraction, b.p. 59.5° at 12 mm, was obtained.

Found %: C 8.78, 8.73; H 2.24, 2.54; total Cl 46.88, 46.85; hydrolyzable Cl 46.89, 46.87; P 22.19, 22.28; M 146.1. CH_3OPOCl_2. Calculated %: C 8.05; H 2.02; Total Cl 47.65; hydrolyzable Cl 47.65; P 20.81; M 149.

Therefore, the product was the methyl ester of dichlorophosphoric acid. Literature constants: b.p. 62-64° at 14 mm [8].

The ethyl ester of dichlorophosphoric acid (2.5 g), b.p. 163-165°, was obtained in an analogous manner from $POCl_3$ (15.5 g) and diazoethane (8.5 g).

Found %: Total Cl 43.89; Hydrolyzable Cl 43.03; M 159. $C_2H_5OPOCl_2$. Calculated %: Total Cl 43.55; Hydrolyzable Cl 43.55; M 163. The substance – the ethyl ester of dichlorophosphoric acid – was described in the literature [8]: b.p. 167° (with decomp.).

* The diazomethane was dried initially in the usual manner at a temperature of -70° over solid KOH and then over sodium ribbon.

19. Reaction between diazomethane and PCl_5. Trichloromethyl phosphine oxide $(ClCH_2)_3PO$. A solution of 6 g of diazomethane in 200 ml of ether dried in the usual manner over KOH with cooling, was added, dropwise with mechanical stirring, at -40°, to a mixture of 10 g of PCl_5 and 40 ml of dry ether. At end of the formation of the nitrogen, the cooling was removed and the solution was left overnight. The ether solution was poured from the precipitate, which was then extracted with ether (2 times with 50 ml). After the removal of the ether, 6-7 g of needlelike crystals separated, which after recrystallization from gasoline, melted at 100.5°. The product did not contain any chlorine that could be hydrolyzed under ordinary conditions.

Found %: C 18.43, 19.00; H 3.25, 3.43; Cl 54.24; P 15.21, 15.59; M 188. $(ClCH_2)_3PO$. Calculated %: C 18.41; H 3.07; Cl 54.53; P 15.87; M 195.5.

Reported (as the semihydrate) by Hoffmann: m.p. 88-89° [6].

20. Reaction of diazoethane with PCl_5. A dry solution of 14-15g of diazoethane (5 moles) in 400 ml of ether, dried over KOH and then over sodium ribbon, was added (efficient mechanical stirring) at -40 to -50° to 10 g (1 mole) of finely ground PCl_5 in 50 ml of absolute ether. The last portions of the diazoethane decolorized slowly. The solution, containing unreacted diazoethane, was allowed to stand over night at room temperature. All of the PCl_5 dissolved. After distillation of the ether, 10 g of a viscous, cloudy liquid, difficultly soluble in water, containing hydrolyzable chlorine, was obtained. The vacuum distillation (5 mm) of the substance was accompanied by noticeable decomposition, and a homogeneous product could not be isolated. A liquid, b.p. 55-115° at 5 mm, 4.5 g was collected together and hydrolyzed with 5 ml of hot water (very little dissolved in cold water). After 2-3 days, the oily layer was extracted. The water layer was then extracted with ether, the ether extract dried with sodium sulfate, and the ether distilled. The residual oil crystallized on standing in the desiccator. The thin needles were pressed on a plate and recrystallized from a mixture of benzene and gasoline, m.p. 107°. 1.5 g was obtained; it was moderately soluble in water and very soluble in alcohol.

4.614 mg substance: 4.278 mg CO_2; 2.075 mg H_2O. 11.700 mg substance: 6.058 ml 0.02 N $AgNO_3$. Found %: C 25.28; H 5.03; Cl 36.72. $(CH_3CHCl)_2PO(OH)$. Calculated %: C 25.13; H 4.18; Cl 37.17.

The silver salt of di α-chloroethyl-phosphinic acid was water soluble.

21. Aniline salt of di(α-chloroethyl)phosphinic acid. 3 ml of aniline was added to a solution of 2 g of $(CH_3CHCl)_2PO(OH)$ in 50 ml of benzene. The salt precipitated in the form of needles, which decomposed on melting at 160°. The yield was quantitative.

2.815 g substance: 0.1430 ml N_2 (28°, 738 mm). Found %: Cl 5.48.

$(CH_3CHCl)_2PO(OH) \cdot C_6H_5NH_2$. Calculated %: N 4.93.

SUMMARY

1. It was shown that the diazo method for the synthesis of organo-elemental compounds could be successfully extended to the preparation of organophosphorus compounds.

2. Phosphorus trichloride and phosphorus tribromide, when reacted with diazomethane, diazoethane, and diazobutane, formed the corresponding primary α-halodialkylphosphorus compounds, whose properties and derivatives are reported.

3. Phosphorus pentachloride with diazomethane and diazoethane formed the corresponding secondary and tertiary α-halodialkyl phosphorus derivatives. Phosphorus oxychloride and bromide did not form any compounds containing a C-P bond under analogous conditions.

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TRANSFORMATION OF CYCLOPENTENE BY THE ACTION OF ALUMINUM CHLORIDE

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On studying the action of aluminum chloride on cyclohexene, it was found that the reaction proceeded mainly in the direction of the formation of hydropolymers. A small amount of cyclohexene resisted the dehydrogenation and, as a result, tetracyclohexylbenzene [1] was formed. When the investigation of the polymerization of cyclopentene in the presence of aluminum chloride was started, the formation of hydro-and dehydropolymers was also expected; but apparently, when aluminum chloride reacted with cyclopentene, more complex reactions occurred and did not lead to the formation of polymers.

The polymerization of cyclopentene was conducted at 50° with 20% of the catalyst. When the reaction products were distilled, a series of fractions were obtained, corresponding, in molecular weight, to dimers, trimers, and tetramers, but different in their constants, from polycyclopentyls and polycyclopentylcyclopentene, which had been previously obtained synthetically and were reported in the literature [2-7].

The fraction, b.p. 185-186° at 748 mm, corresponding in molecular weight to the dimer, was a colorless liquid with an odor resembling that of the terpenes. In spite of its high boiling point this substance was very volatile. Its constants were very close to the constants of spirocyclodecane (Tables 1 and 2).

Heptabromospirocyclodecane, b.p. 252.5-253.5°, was prepared by the action of bromine on the above spirocyclodecane. No depression was obtained in a mixed melting point determination with heptabromospirocyclodecane prepared from synthetic spirocyclodecane.

Spirocyclodecane, has, up to now, been prepared synthetically. Zelinsky and Shuikin [7], synthesized it from 1,1'-di-hydroxydicyclopentene; Marvel and Brooks [8] by the cyclization of penta-1,4-dienylcyclopentane followed by hydrogenation. Several spirans have been obtained by means of aluminum chloride but all of these were formed by the isomerization of alicyclic olefins containing substituted arylalkyls in the molecule. The ring was obtained by the fusion of the aromatic ring to the alicyclic olefin at the double bond.

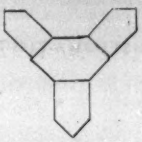
TABLE 1

Name	Formula	Melting point	n_D^{20}	d_4^{20}	Iodine number
Spirocyclodecane	$C_{10}H_{18}$	185-186° 748 mm	1.4740	0.8827	2.87
Tricyclopentane	$C_{15}H_{24}$	127-129 4.5 mm	1.5085	0.9606	2.63
Tetracyclopentane	$C_{20}H_{32}$	198-200 4.5 mm	1.5295	1.0028	3.5
Hexacyclopentene	$C_{30}H_{48}$		–	–	36.2

Thus, the possibility of forming spirocyclodecane by the polymerization of cyclopentene in the presence of aluminum chloride was shown in this investigation. It is believed that a dimer is formed during the polymerization, one ring of which, under the isomerizing action of aluminum chloride, is transformed into a six-membered ring at the carbon atom of the other five-membered ring. Since it is energetically impossible to transform a five membered ring into a four-membered one [9] in this case, a system of a five-membered and six-membered ring with one common carbon atom is formed – spirocyclodecane.

The fraction, b.p. 127-129° at 4.5 mm, according to its molecular weight, was tricyclopentane with an iodine number of 2.63 (Table 1). This substance can practically be considered saturated because, with one

double bond, it would have had an iodine number of 124.5. The elementary analysis corresponded to the formula $C_{15}H_{24}$. The following structure is considered to be probable for this compound:



The fraction with b.p. 198-200° at 4.5 mm and iodine number 3.5, was the tetramer, according to its molecular weight. A formula $C_{20}H_{32}$ was calculated from the elementary analysis, whereas, the formula $C_{20}H_{34}$ corresponds to the saturated tetramer. The iodine number was insignificant. Apparently, as in the case of the trimer, the lack of two hydrogens was not due to the presence of a double bond (theoretical iodine number 83.4), but was a result of the fusion of rings to form a new ring.

TABLE 2

Reference	Boiling point	n_D^{20}	d_4^{20}	MR_D	
				Calculated	Found
[7]	185-186°	1.4748	0.8877	43.98	43.74
[8]	184-186.5	1.4744	0.8805	43.98	44.14
Our results	185-186	1.4740	0.8827	43.98	43.98

The fraction, b.p. 190-220° at 3 mm was a very dense oil with a very abrupt temperature-viscosity curve. Viscosity index: −55. This fraction was not studied in detail.

After distillation of the polymerization products there always remained in the flask a large amount of a glasslike solid residue, which, by means of recrystallization from isopropyl alcohol, gave a finely crystalline substance, m.p. 71-72° and an iodine number 36.2 (Margosches). Further investigation showed that it was the hexamer of cylcopentene, $C_{30}H_{48}$, containing one double bond.

EXPERIMENTAL

Cyclopentene was obtained by the dehydration of cyclopentyl alcohol with orthophosphoric acid at 240°. It had a b.p. of 44°, d_4^{20} 0.7715; n_D^{20} 1.4231.

The apparatus for the polymerization was equipped with a mercury sealed stirrer and an efficient coil condenser connected to a trap immersed into a dish of solid carbonate. The polymerization of cyclopentene was effected at 50° for 30 hours with 20% $AlCl_3$. In spite of the rapid formation of the complex of cyclopentene and aluminum chloride, the rate of polymerization was very slow, and it was necessary to conduct the process at room temperature for 2 days, for 3 hours at 35°, and for 27 hours at 50°. At the end of the polymerization, the upper layer was separated from the solid (complex) lower layer. After washing and drying, the upper layer was fractionated at ordinary pressure and in vacuum. A solid residue, the main portion of the products, remained in the flask.

6 experiments on the polymerization of cyclopentene were conducted. In all cases, the yield of the fraction boiling up to 200° did not exceed 5%; 50% of the product was distributed amont fractions boiling from 80 - 235° at 5 mm. The residue, amounting to 45%, was a solid product.

For example: 74 g of cyclopentene and 14.8 g of $AlCl_3$ were heated for 30 hours at 50°. 50 g of an upper layer was obtained, which on distillation, gave the following fractions: at 748 mm 182-193° − 2.6 g; at 5 mm 80-195° − 13.4 g, 195-235° − 12.2 g (oil), 235-260° − 10.2 g (solid), and residue − 11.6 g.

All of the polymerization products had low iodine numbers which in several cases were equal to zero. The smallest values were found for the lower fractions. The higher boiling fractions had higher iodine values.

After many refractionations, the following fractions were obtained and studied: b.p. 185-187° at 743.7 mm; b.p. 125-129° at 4 mm; b.p. 197-209° at 5 mm; b.p. 190-220° at 3 mm; and a solid residue.

Spirocyclodecane. After a careful distillation of the fraction, a product, b.p. 185-187° at 743.7 mm, was isolated. It was very volatile and had a characteristic odor resembling that of the terpenes.

d_4^{20} 0.8906; n_D^{20} 1.4756. MR_D 43.71; calculated 43.98; iodine number 18.22.

The product b.p. 185-187°, was treated with one volume of sulfuric acid (density = 1.84) for 30 minutes to remove unsaturated impurities. A substance with the following constants was obtained from the acid-treated product:

B.p. 185-186° at 748 mm; d_4^{20} 0.8827; n_D^{20} 1.4740. MR_D 43.98; calculated 43.98; iodine number 2.87.

2.727 mg substance: 8.665 mg CO_2; 3.192 mg H_2O. 2.617 mg substance; 8.320 mg CO_2; 3.130 mg H_2O. 0.1658 g substance; 19.85 g benzene: Δt 0.315°. 0.2617 g substance; 19.85 g benzene: Δt 0.514°. Found %: C 86.71, 86.76; H 13.10, 13.38; M 135.8, 136.3. $C_{10}H_{18}$. Calculated %: C 86.87; H 13.3; M 138.14.

This hydrocarbon was spirocyclodecane according to these constants.

The spirocyclodecane was brominated (according to Gustavson). The bromide, after recrystallization from benzene, was obtained in the form of soft needles, m.p. 252.5-253.5°.

0.0365 g substance: 0.0696 g AgBr (Carius); 0.0562 g substance: 0.1064 g AgBr. Found %: Br 81.14, 80.57. $C_{10}H_{18}Br_8$. Calculated %: Br 81.02.

A smooth analysis was obtained only with small samples. When the size of the sample was increased, the tubes usually exploded. The spirocyclodecane heptabromide was identical with the synthetic spirocyclopentyl heptabromide prepared by N.V. Elagena at Moscow State University. The synthetic spirocyclodecane (cyclopentenspirocyclohexane) had an m.p. of 250°. The mixed melting point with spirocyclodecane heptabromide obtained from the polymerization of cyclopentene did not give any depression.

Tricyclopentane. A narrow boiling fraction, b.p. 125-129° at 4.5 mm, was isolated from the fraction with b.p. 80-195° at 5 mm by means of a large number of redistillations: d_4^{20} 0.9622; n_D^{20} 1.5098; iodine number 13.84.

The product was treated three times with one volume of sulfuric acid (d = 1.84) to remove the unsaturated compounds. Each of the sulfonations lasted 30 minutes. After neutralizing and drying, the product was distilled and a fraction, b.p. 127-129° at 4.5 mm, was isolated from it. It had the following constants:

d_4^{20} 0.9606; n_D^{20} 1.5085. MR_D 63.41; calculated 62.67.

3.015 mg substance: 9.715 mg CO_2; 3.258 mg H_2O. 2.572 mg substance: 8.300 mg CO_2; 2.730 mg H_2O. 0.1492 g substance: 20.45 g benzene: Δt 0.185°. 0.2488 g substance; 20.45 g benzene: Δt 0.308°, Found %: C 87.93, 88.07; H 12.09, 11.88; M 201.9, 202.2. $C_{15}H_{24}$. Calculated %: C 88.15; H 11.85; M 204.19.

Tetracyclopentane. $C_{20}H_{32}$. The fraction with b.p. 197-202° at 5 mm, was treated 5 times with one volume of sulfuric acid (d = 1.84) to remove the unsaturated compound impurities. The iodine number decreased from 7.14 to 3.5.

The purified product had the b.p. 198-200° at 4.5 mm and the following constants:

d_4^{20} 1.0028; n_D^{20} 1.5295. MR_D 83.76; calculated 83.56.

2.530 g substance: 8.170 mg CO_2; 2.710 mg H_2O. 2.520 mg substance: 8.135 mg CO_2; 2.712 mg H_2O. 0.2350 g substance: 21.26 g benzene: Δt 0.212.° 0.3764 g substance: 21.26 g benzene: Δt 0.340°. Found %: C 88.12, 88.10; H 11.98, 12.04; M 267.0, 266.6. $C_{20}H_{32}$. Calculated %: C 88.15; H 11.85; M 272.26.

The fraction with b.p. 190-220° at 3.5 mm was an oil which had the following constants:

d_4^{20} 1.0038; n_D^{20} 1.5322; iodine number 9.24; M 291.8.

2.688 mg substance: 8.675 mg CO_2; 2.900 mg H_2O. 2.853 mg substance: 9.200 mg CO_2; 3.075 mg H_2O. Found %: C 88.07, 88.00; H 12.07, 12.06.

Viscosity at 50° − 80.49 cst., at 100° − 9.01 cst. (E_{50} 10.6; E_{100} 1.75). Viscosity index − 55. Freezing point -3°.

Hexacyclopentene. A finely crystalline substance, m.p. 71-72°, and iodine number (Margosches) 36.2, was obtained after the recrystallization of the solid residue from isopropyl alcohol. The theoretical iodine number for $C_{30}H_{48}$ is 62.20. The decrease in the iodine number, apparently, was due to the instability of the iodide of hexacyclopentane.

2.610 mg substance: 8.425 mg CO_2; 2.770 mg H_2O. 2.471 mg substance: 7.974 mg CO_2; 2.618 mg H_2O. 0.0919 g substance: 19.23 g benzene: Δt 0.060°. 0.0818 g substance: 24.60 g benzene: Δt 0.048°. Found %: C 88.08, 88.07; H 11.88, 11.86; M 407.8, 398.1. $C_{30}H_{48}$. Calculated %: C 88.15; H 11.85; M 408.38.

Therefore, this product is a hexacyclopentene containing one double bond.

SUMMARY

A complex mixture of hydrocarbons results from the reaction of cyclopentene with aluminum chloride, from

which spirocyclodecane, tricyclopentane, tetracyclopentane, and hexacyclopentene was isolated.

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PREPARATION OF DIMETHYL PYROCARBONATE

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The literature reports the synthesis of four examples of esters of the hypothetical pyrocarbonic acid; diethyl pyrocarbonate, di-n-propyl pyrocarbonate [1], di-n-butyl pyrocarbonate [2], and methyl ethyl pyrocarbonate [3]. The attempts of Boehm and Mehta to prepare dimethyl pyrocarbonate by their method failed. The negative results of the experiments were explained by these authors as being due to the thermal instability of dimethyl pyrocarbonate, which, during the isolation of the crude product by vacuum distillation, completely decomposed into carbon dioxide and dimethyl carbonate.

The method of Boehm and Mehta was followed closely in the experiment conducted to verify this conclusion, the only difference being that the vacuum distillation of the crude product was replaced by one at ordinary pressure, because the decomposition products of dimethyl pyrocarbonate could more easily and accurately be determined in this fashion. The formation of carbon dioxide and dimethyl carbonate occurred only in insignificant amounts. The main fraction obtained was methyl alcohol. Apparently, dimethyl pyrocarbonate was present in the crude reaction product. It must be pointed out that the method of Boehm and Mehta is based on the reaction of chlorocarbonic esters with emetine in chloroform, and the saponification of the carboalkoxy derivatives of emetine with aqueous potassium hydroxide. Under their conditions, the formation of methyl alcohol is possible, either by the saponification of the carbomethoxy derivative of emetine at the ester linkage, or by the saponification of the initially formed dimethyl pyrocarbonate. In any case, it is clear that the reason for the negative results in the synthesis of dimethyl pyrocarbonate by this method, was the presence of a strong hydrolyzing agent in the reaction medium. Dimethyl pyrocarbonate must be more susceptible to hydrolysis than diethyl pyrocarbonate, since the latter is obtained in good yield by the method of Boehm and Mehta.

A new method for the preparation of pyrocarbonic esters was suggested by the authors [3], which was based on the reaction of the alkali salts of alkyl carbonic acid with chlorocarbonic esters. It excluded the presence of hydrolyzing factors in the reaction medium. It was shown that the considerable increase in yield of diethyl pyrocarbonate by this synthesis over that of Boehm and Mehta, was due to this fact. Experiments conducted to develop this method led to fully satisfactory yields of up to 64% of the theoretical.

Dimethyl carbonate was a colorless, readily volatile oil, with a pleasant, slightly sharp odor, insoluble in water, but readily soluble in ether, alcohol and benzene. In contrast to all of the pyrocarbonates prepared up to now, dimethyl pyrocarbonate crystallized readily on cooling.

The structure of dimethyl pyrocarbonate is established by its formation from the reaction between alkali salts of methyl carbonic acid and methyl chlorocarbonate (Equation 1), by its decarboxylation on pyrolysis (Equation 2), and by its reaction with ammonia and aniline to form the corresponding urethane and phenyl urethane (Equations 3 and 4).

$$CH_3O{-}CO{-}ONa + Cl{-}CO{-}OCH_3 \longrightarrow CH_3O{-}CO{-}O{-}CO{-}OCH_3 + NaCl \quad (1)$$

$$CH_3O{-}CO{-}O{-}CO{-}OCH_3 \xrightarrow{123\text{-}149^\circ} CH_3O{-}CO{-}OCH_3 + CO_2, \quad (2)$$

$$CH_3O{-}CO{-}O{-}CO{-}OCH_3 + NH_3 \longrightarrow CH_3O{-}CO{-}NH_2 + CH_3OH + CO_2 \quad (3)$$

$$CH_3O{-}CO{-}O{-}CO{-}OCH_3 + C_6H_5NH_2 \longrightarrow CH_3O{-}CO{-}NHC_6H_5 + CH_3OH + CO_2 \quad (4)$$

A comparative study of the hydrolysis of dimethyl and diethyl pyrocarbonate showed that dimethyl pyrocarbonate hydrolyzed much more rapidly than diethyl pyrocarbonate.

The following equations are proposed on the basis of the study of hydrolysis in water and aqueous alkali:

$$RO{-}CO{-}O{-}CO{-}OR + HOH \longrightarrow 2ROH + 2CO_2,$$

$$RO{-}CO{-}O{-}CO{-}OR + 4KOH \longrightarrow 2ROH + 2H_2CO_3 + H_2O.$$

Dimethyl pyrocarbonate is less stable thermally than diethyl pyrocarbonate.

EXPERIMENTAL

1. Synthesis of dimethyl pyrocarbonate by the method of Boehm and Mehta. The methyl chlorocarbonate necessary for the synthesis was prepared by the method of Dumas [4]. The boiling point of the ester (71-72°) corresponded to the literature value. A solution of 1 g of emetine hydrochloride (pharmacopoeia preparation) in 30 ml of chloroform and 4.7 g of methyl chlorocarbonate were mixed in a separatory funnel. 27 ml of a 10% aqueous potassium hydroxide was added, with good shaking and water cooling, in three 9-ml portions, to this mixture. After addition of all the alkali, the reaction mixture was slightly alkaline. The chloroform layer was separated and the chloroform distilled on the water bath; the residue, after removal of the chloroform, was processed with ether; a yellow precipitate formed and was filtered off; the filtrate was treated with dilute hydrochloric acid. The ether layer was then separated and dried over fused sodium sulfate for several hours; the ether was distilled and the residue fractionated in vacuum. 2 - 3 drops of a liquid distilled at 55° and 8 mm.

In other experiments, the residue obtained after the distillation of the ether was fractionated at ordinary pressure. A large portion of the liquid distilled at 60-68° (methyl alcohol) and an almost insignificant amount – several drops in all – at 90-91° (dimethyl carbonate); during the distillation there was a constant evolution of a small amount of carbon dioxide.

2. Synthesis of dimethyl pyrocarbonate from methyl chlorocarbonate and sodium methylcarbonate. Methyl chlorocarbonate was prepared in the same way as in the previous case. Sodium methyl carbonate was prepared by passing dry carbon dioxide into a solution of sodium methylate in methyl alcohol. The purity of the salt was shown by its analysis for sodium content: found – 23.42% sodium; calculated – 23.37%. A mixture of 9.8 g of sodium methylcarbonate and 37 g of methyl chlorocarbonate was placed into a 100-120 ml tall beaker, equipped with a reflux condenser with a calcium chloride tube and a mercury-sealed, mechanical stirrer. The reaction mixture was then filtered through a Buchner funnel and the residue washed with a small amount of dry ether. After removal of the ether, the filtrate was fractionated in vacuum. The excess chlorocarbonic ester distilled at 25-30° at 110 mm; the residue distilled completely at 45-46° and 5 mm. Yield 8.5 g or 63.43% of the theoretical. When it was cooled with ice water and shaken, the ester rapidly crystallized in the form of colorless prisms.

Freezing point 15.2°; d_4^{20} 1.2585; n_D^{20} 1.3950.

0.2108 g substance: 0.2768 g CO_2; 0.0836 g H_2O. Found %: C 35.81; H 4.44. $C_4H_6O_5$. Calculated %: C 35.84; H 4.51.

3. Pyrolysis of dimethyl pyrocarbonate. The pyrolysis was effected in a 4-5 ml flask with a ground-in, well-fitted, reflux condenser, the top of which was connected to a potassium hydroxide apparatus. The neck of the flask was closed with a two-hole stopper. Through one of the holes a thermometer was fitted with its bulb almost touching the bottom of the flask, and in the other hole, a glass tube with a valve for the passage of air. 3.70 g of dimethyl pyrocarbonate was weighed into the flask. After passing dry, carbon dioxide-free air through the apparatus for 15 minutes, it was connected to the potassium hydroxide apparatus containing 50% potassium hydroxide. The flask was heated on a glycerin bath. Bubbles of gas started forming in perceptible amounts, and rapidly increased, at 123°. The temperature of the liquid in the flask gradually rose to 149° and then began to drop; at 95°, the evolution of the CO_2 ceased. 1.20 g of carbon dioxide was collected; calculated from the equation of the pyrolysis: 1.21 g; the residue in the flask weighed 2.41 g; the calculated weight of the dimethyl carbonate from the pyrolysis equation was 2.48 g.

The residual liquid in the flask distilled completely at 90-91°, which corresponded to the boiling point reported in the literature for dimethyl carbonate [5].

Found %: C 39.89; H 6.80. $C_3H_6O_3$. Calculated %: C 40.00; H 6.71.

4. Pyrolysis of diethyl pyrocarbonate. The pyrolysis of diethyl pyrocarbonate was effected in the same apparatus and under the same conditions as the pyrolysis of dimethyl pyrocarbonate. The formation of the gas bubbles was perceptible at 155°; the temperature of the liquid gradually rose to 175° and then began to fall; at 130°, the evolution of carbon dioxide ceased.

Sample of diethyl pyrocarbonate – 4.75 g; collected CO_2 – 1.24 g; calculated from the pyrolysis equation 1.29 g. The residue in the flask weighed 3.40 g; calculated amount of diethyl carbonate from the pyrolysis equation 3.46 g. The residue in the flask distilled completely at 125-126°, which corresponded to the distillation temperature of diethyl carbonate.

5. Urethane (methyl ester of carbamic acid). A saturated solution of ammonia in ethyl alcohol was added to 1 g of dimethyl pyrocarbonate. The reaction started and continued rapidly. The mixture heated up and carbon dioxide was given off. The ammonia was added until the evolution of the carbon dioxide ceased. After evaporation of the alcohol, colorless crystals remained, which were dried in a desiccator over calcium chloride. M.p. 52-53°; according to Gattermann [7], 52°; according to Schmidt [8], 54.2°.

Found %: N 18.35. $C_3H_7O_2N$. Calculated %: N 18.65.

The reaction proceeded much more violently with gaseous ammonia.

6. Phenyl urethane (methyl ester of phenyl carbamic acid). 1 g of dimethyl pyrocarbonate was added, dropwise, to 0.7 g of freshly distilled aniline. The reaction started and proceeded rapidly, with the mixture heating up and the evolution of carbon dioxide. After cooling, the mixture crystallized completely, either when it was shaken, or when it was seeded with a crystal of phenyl urethane. The yield was quantitative. On recrystallization from hot water, the phenyl urethane was obtained in the form of scaly crystals, m.p. 47°, which agreed fully with the literature [9].

7. Hydrolysis of dimethyl pyrocarbonate and diethyl pyrocarbonate. The apparatus used for the hydrolysis consisted of a beaker [a] 50-75 ml in volume, fitted with a mercury-sealed, mechanical stirrer and two connected burets fitted to the beaker by means of glass tubes. A saturated solution of sodium chloride, which was equal to one-half the total volume of the bufets (with a small excess), was placed into the burets. One of the burets (b), fitted with a three-way stopcock, was used to collect the carbon dioxide generated during the hydrolysis, the other (c) was always left open to the atmosphere in order to level the liquid in the first buret to zero and to keep the pressure inside the apparatus equal to that of the atmosphere. The experiments were performed at room temperature (15°). In order to exclude the influence of the variation in temperature, the beaker was placed in a constant temperature water bath.

a) 10 ml of distilled water was placed in the beaker and initially saturated with carbon dioxide for 10 minutes. The liquid level in the first buret was brought to zero and the corresponding opening in the three way stopcock placed at "closed" position. The stirrer was allowed to run (100-120 r.p.m.). After the excess carbon dioxide stopped separating, the stirrer was stopped and 0.0618 g of dimethyl pyrocarbonate was introduced through the side tube with a special pipet. The side arm was plugged with a plastic stopper, the liquid in the first buret was again leveled to zero, and the stirrer allowed to run at the previous rate. The formation of carbon dioxide stopped after 90 minutes. A total of 20.3 ml (reduced to normal conditions) of gas was collected; calculated frm the hydrolysis equation 20.6 ml.

Hydrolysis of dimethyl and diethyl pyrocarbonate

Time from beginning of expt. (minutes)	Formation of carbon dioxide on hydrolysis			
	Dimethyl pyrocarbonate		Diethyl pyrocarbonate	
	in ml	In % of the quantity calculated from the hydrolysis equation	in ml	In % of the quantity calculated from the hydrolysis equation
15	8.1	41.26	4.3	26.88
30	13.7	66.51	6.5	40.63
60	17.7	85.92	10.0	62.50
90	20.3	98.54	12.4	77.50
120	–	–	14.4	90.00
150	–	–	15.9	99.37

b) 0.0580 g of diethyl pyrocarbonate was hydrolyzed under approximately analogous conditions. The formation of the carbon dioxide ceased after 150 minutes. A total of 15.9 ml (reduced to normal conditions) of gas was collected; calculated from the hydrolysis equation – 16 ml.

The data on the dynamics of the formation of carbon dioxide are listed in the Table.

8. Hydrolysis of dimethyl pyrocarbonate and diethyl pyrocarbonate with aqueous potassium hydroxide. The aqueous solution of potassium hydroxide was 0.3685 N; 1 ml corresponded to 0.01294 g of dimethyl pyrocarbonate or 0.01493 g of diethyl pyrocarbonate.

a) 50 ml of potassium hydroxide solution was added rapidly to 0.2320 g of dimethyl pyrocarbonate with good stirring; the ester dissolved within the first minute. 10 ml of the solution was removed and rapidly titrated with hydrochloric acid.

The titration was effected according to Warder [10]. 18.5 ml of potassium hydroxide, corresponding to 0.2287 g of dimethyl pyrocarbonate, was consumed during the saponification. The ester hydrolyzed to an extent of 93.4%.

b) A 0.3983 g sample of diethyl pyrocarbonate was saponified with the alkali under the same conditions as the dimethyl pyrocarbonate. 26 ml of potassium hydroxide, corresponding to 0.3882 g of diethyl pyrocarbonate, was consumed during the saponification of the ester. Diethyl pyrocarbonate hydrolyzed to an extent of 98.8%.

SUMMARY

1. A method is given for the preparation of dimethyl pyrocarbonate, which is not reported in the literature.

2. The comparative characterization of dimethyl- and diethyl- pyrocarbonate, on the basis of thermal and hydrolysis stability, is given.

3. A new method for the preparation of urethane and N-substituted urethanes is given.

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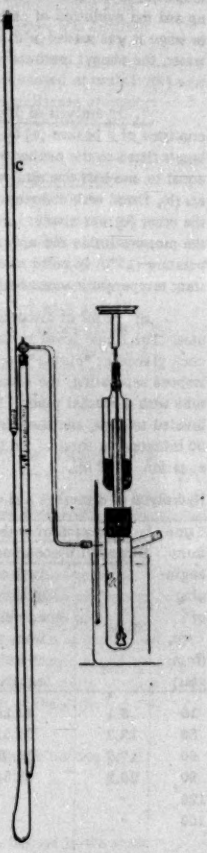
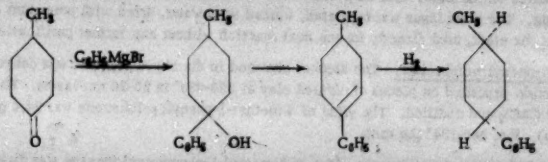


CYCLIZATION OF AROMATIC COMPOUNDS

V. SYNTHESIS OF 1-METHYL-4-PHENYLCYCLOHEXANE

N. G. Sidorova and A. D. Grebenyuk

There are many difficulties in the investigation of the condensation products of isomeric methylcyclohexanols and benzene because of the possibility of many isomeric and stereoisomeric forms, and the lack of study of this series of hydrocarbons. The synthesis of individual "model" hydrocarbons is of considerable importance for decreasing the difficulties in the investigation of structure and configuration of the condensation products. One of these hydrocarbons, trans-1-methyl-4-phenylcyclohexane was synthesized in the following manner:



This method was generally used for the synthesis of substituted cyclohexyl hydrocarbons. A 1-methyl-4-phenylcyclohexane, of unknown configuration was synthesized in this manner [1]. The last part of this synthesis – the hydrogenation – was effected by these authors at 36° and 85 atm. of hydrogen over nickel on kieselguhr. It is believed that at such low temperature, the cis product was formed mainly, or almost exclusively.

When aromatic compounds or cycloalkenes are hydrogenated, the preference of one form over the other depends on the medium and the temperature. Skita [2], generalizing a large amount of experimental material on hydrogenation with platinum catalysts, proposed rules for the effect of the media on the configuration of the hydrogenation product; hydrogenation in acidic media preferably leads to the formation of the cis isomer and in basic or neutral media to the trans isomer. The preference of one form over the other also can depend on the temperature. For example, Zelinsky and Margolis [3], upon the hydrogenation of o- and p-acids over osmium catalysts at 50 - 70°, obtained cis-dimethylcyclohexanes and at 150° mixtures of stereoisomers with considerable amounts of the trans forms. The effect of the temperature on the direction of the hydrogenation with platinum on carbon can also be seen in the work of Kazansky, et al, on the synthesis and hydrogenative cleavage of cyclodi- and tri-substituted cyclopentenes. On the synthesis of 1,2-dimethyl and 1,2,3-trimethylcyclopentanes [4,5], by hydrogenation of the corresponding cyclo-olefins at 130-140°, a mixture of cis and trans isomers was obtained. On hydrogenation of each of the stereoisomeric 1,2,3-trimethylcyclopentenes with the same catalyst at 300-310°, along with hydrogenolysis, mutual steric rearrangements took place which favored the complete formation of the trans form [6]. The results of the hydrogenation with nickel will probably also depend on the temperature.

The hydrogenation of cyclic hydrocarbons with nickel at 180° usually leads completely to, or favors, the trans form [7]. For this reason, the above temperature was chosen for the hydrogenation of 4-methyl-1-phenylcyclohexene with Raney nickel. However, this high temperature is not completely convenient because, under these conditions, the aromatic ring also hydrogenates; for this reason, the hydrocarbons contained 1-methyl-4-cyclohexylcyclohexane as an impurity, as seen from the constants.

The synthesized hydrocarbon was characterized by the preparation of acetamino- and phenylamino derivatives, and by comparing them with the corresponding derivatives of the hydrocarbon obtained by the American chemists. The melting points of our derivatives of the hydrocarbon (see Table) were higher than the melting points of the corresponding derivatives of their hydrocarbon; indicating that the 1-methyl-4-phenylcyclohexane synthesized had the trans configuration.

Melting points of the derivatives of the stereoisomeric 1-methyl-4-phenylcyclohexanes.

Configuration	Acetoamino derivative	Phenylamino derivative
Cis isomer	142°	197°
Trans isomer	157 - 158	207 - 208°

However, the hydrocarbon probably was not the pure trans form because many recrystallizations of the derivatives were needed to obtain constant melting points.

EXPERIMENTAL

4-Methylcyclohexanol was obtained by the hydrogenation of p-cresol over Ni (Raney) at 180° and 120 atm. hydrogen pressure. B.p. 166-167° (720 mm). The subsequent steps in the synthesis differed somewhat in conditions and the yields from those reported in the literature [1].

4-Methylcyclohexanone. A solution of 40 g of sodium dichromate in 25 ml of H_2SO_4 and 90 ml of water was added, dropwise with stirring, to a solution of 45 g of 4-methylcyclohexanol heated to 40-50°. After the addition, the heating was continued for one hour at this temperature. The ketone was separated, washed with water, sodium carbonate solution, and again with water; and dried with $CaCl_2$ and distilled. The yield was 27.3 g (61.7% of theory). B.p. 169-169.5° (725 mm).

4-Methyl-1-phenylcyclohexanol. 26.6 g of 4-methylcyclohexanone was added dropwise over 3 hours to C_6H_5MgBr prepared from 48 g of phenyl bromide, 7.5 g of magnesium, and 120 ml of absolute ether; the mixture was then heated on the water bath for 2 hours. The decomposition was effected with dilute hydrochloric acid with ice cooling. The ether layer was separated, washed with water, dried with potassium carbonate, and after the removal of the ether, used directly for the next reaction without any further purification.

4-Methyl-1-phenylcyclohexene. The alcohol obtained in the above reaction was dehydrated by passing it over aluminum oxide deposited on pieces of unfused clay at 320-330° in 25-30 cm layers. The reaction product was dried over $CaCl_2$ and distilled. The yield of 4-methyl-1-phenylcyclohexene was 24.4 g (60 % of theory based on the ketone). B.p. 130-134° (15 mm).

Trans 1-methyl-1-phenylcyclohexane. 15 g of 4-methyl-1-phenyl-cyclohexane was dissolved in 10 ml of ethyl alcohol and mixed with 1.5 g of Ni (Raney) in an autoclave. The air in the autoclave was replaced with hydrogen and heating started. As soon as the temperature rose to 180°, 65 atm. of hydrogen was pumped in and the stirring started. The amount of hydrogen absorbed was somewhat greater than that theoretically calculated. After separation of the catalyst and removal of the alcohol, the product was distilled over metallic sodium.

B.p. 249-250° (727 mm); d_4^{20} 0.9277; n_D^{20} 1.5180; MR_D 56.88; calculated 56.43.

0.1196 g substance: 0.3912 g CO_2; 0.1120 g H_2O. Found %: C 89.22; H 10.40. $C_{13}H_{18}$. Calculated %: C 89.65; H 10.35.

According to the amount of hydrogen absorbed and the constants, it is seen that the hydrocarbon contained methylcyclohexylcyclohexane as an impurity.

For the characterization of trans 1-methyl-4-phenylcyclohexane, the entire product of the hydrogenation was nitrated, in the usual manner, without any initial separation, and the nitro compound was reduced with tin and hydrochloric acid. At the end of the reduction, the unreacted hydrocarbon and traces of the nitro compound were steam distilled. An excess of alkali was added to the residue, and the amine was steam distilled. The distillate was saturated with salt and the amine extracted with benzene. After drying with potassium hydroxide and removing the benzene, the amine was distilled. The yield of p-(4-methylcyclohexyl)aniline was 50.7% calculated on the hydrocarbon. B.p. 190-198° (at 38 mm).

Acetanilide – m.p. 157-158° (from dilute alcohol)

Benzanilide – m.p. 207-208° (from alcohol). 3.75 mg substance: 0.160 ml N_2 20.5° (726 mm). Found %: N 4.74. $C_{20}H_{23}ON$. Calculated %: N 4.78.

SUMMARY

1. It was shown that the hydrogenation of 4-methyl-1-phenyl-cyclohexene at 180°, with Ni (Raney), favored the formation of the trans isomer of 1-methyl-4-phenylcyclohexane.

2. p-(Trans 4-methylcyclohexyl)acetanilide and benzanilide were prepared.

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ALLYLIC REARRANGEMENTS

XVII. REACTION BETWEEN ORGANO-MAGNESIUM COMPOUNDS AND ISOMERIC METHOXYCHLOROPENTENES

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In previous communications on the study of the reaction between organo-magnesium compounds and certain isomeric alkoxychloropentenes, it was shown that they proceed, to a great extent or fully, by the ionic mechanism. It was also shown that, varing with the nature of the radicals forming the organo-magnesium compounds and the isomeric alkoxycyclopentenes, mixtures of products are formed which differ considerably in their composition. For example, the reaction between phenyl magnesium bromide and the isomeric methoxychloropentenes leads to the formation of identical mixtures of isomeric methoxyphenylpentenes; whereas the reaction between phenyl magnesium bromide and the isomeric butoxychloropentenes gives only one product, 1-butoxy-5-phenylpent-3-ene, the primary chloride according to its structure.

The reaction of ethyl magnesium bromide and butyl magnesium with the isomeric ethoxychloropentenes and butoxychloropentenes leads to the formation of mixtures of two products, the corresponding 1-alkoxy-5-alkylpent-3-enes, derived from the primary form of the allyl halide, and the 1-alkoxy-6-β-alkoxyethylocta-3,7-dien, derived from the primary and secondary form of the allyl halide. The latter compounds are also formed by the direct action of metallic magnesium on the above isomeric alkoxychloropentenes; an abnormal bimolecular mechanism was proposed to explain their formation.

In the present study, the reaction between isomeric methoxychloropentenes, the most simple of the alkoxychloropentenes, and a series of organo-magnesium compounds was studied in order to obtain more detailed and more complete information on this theoretically interesting reaction, and to increase the amount of factual material. The organo-magnesium compounds used were benzyl magnesium chloride, ethyl magnesium bromide, and butyl magnesium bromide. Three products resulted from the action of benzyl magnesium chloride on 1-methoxy-5-chloropent-3-ene: 1-methoxy-3-benzylpent-4-ene, 1-methoxy-5-benzylpent-3-ene, and dibenzyl. The total yield of the isomeric methoxybenzylpentenes was 60.1%. 1-Methoxy-3-benzylpent-4-ene constituted 34.7% and 1-methoxy-5-benzylpent-3-ene 65.3% of the mixture. Similar results were obtained from the analogous reaction of benzyl magnesium with 1-methoxy-3-chloropent-4-ene. The total yield of the isomeric methoxybenzylpentenes was 51%; the mixture consisted of 35% of 1-methoxy-3-benzylpent-4-ene and 65% of 1-methoxy-5-benzylpent-3-ene. The formation of a considerable amount of dibenzyl occurred. The structure of these compounds was determined by oxidizing them with potassium permanganate. Benzoic and formic acids were isolated from the oxidation of 1-methoxy-3-benzylpent-4-ene, and benzoic and methoxypropionic acids from 1-methoxy-5-benzylpent-3-ene. It is seen from the above experiment that the reaction of benzyl magnesium chloride with both of the isomeric methoxychloropentenes forms a similar mixture of isomeric methoxybenzylpentenes. These results lead to the conclusion that both of these reactions occur by means of the same ionic mechanism. Later, the reactions of isomeric methoxychloropentenes with ethyl magnesium bromide were studied. Two products resulted from the action of ethyl magnesium bromide on 1-methoxy-5-chloropent-3-ene: 1-methoxyhept-3-ene in a 55.3% yield and 1-methoxy-6-β-methoxyethyloct-3,7-dien in a 19% yield. These same products, in yields of 63.1% and 22.3% respectively, were obtained from the reaction of ethyl magnesium bromide with 1-methoxy-3-chloropent-4-en. The structure of the products was determined by oxidizing them with potassium permanganate. The glycol, 1-methoxy-hept-3,4-diol was obtained by the oxidation of 1-methoxy-hept-3-en with the calculated amount of potassium permanganate under mild conditions, according to Wagner, and butyric and methoxypropionic acids under more drastic conditions. 1-Methoxy-3,4-dibromoheptane was obtained in 62.2% yield by the addition of bromine to 1-methoxyhept-3-en. Analogous results were obtained by reaction of the isomeric methoxychloropentenes with butyl magnesium bromide. 1-Methoxynon-3-ene in 58.9% yield and 1-methoxy-6-β-methoxyethylact-3,7-dien in 6.9% yield were obtained from 1-methoxy-5-chloropent-3-en. The same products in similar yields were obtained from the reaction of butyl magnesium bromide with 1-methoxy-3-chloropent-4-en. The

glycol, 1-methoxynon-3,4-diol was obtained by the oxidation of 1-methoxynon-3-en with potassium permanganate and 1-methoxy-3,4-dibromononane by its bromination. The results obtained agreed with those obtained previously in analogous experiments with isomeric ethoxychloropentenes and butoxychloropentenes. Evidently, the stages of the reactions in which 1-methoxyhept-3-en and 1-methoxynon-3-en are formed from both of the isomeric methoxychloropentenes occur by means of an ionic mechanism which is analogous to the one proposed above for the reaction with benzyl magnesium chloride.

The formation of 1-methoxy-6-β-methoxyethyloct-3,7-dien in the reaction of ethyl magnesium bromide and butyl magnesium bromide with the isomeric methoxychloropentenes can be explained by the occurrence of an exchange reaction between them, leading to the formation of the organo-magnesium compound from the methoxychloropentenes, as an intermediate.

$$CH_3OCH_2CH_2CH{=}CHCH_2Cl + C_2H_5MgBr \rightarrow CH_3OCH_2CH_2CH{=}CHCH_2MgBr$$

$$CH_3OCH_2CH_2CH{=}CHCH_2MgBr + ClCH_2CH{=}CHCH_2CH_2OCH_3 \rightarrow CH_3OCH_2CH_2\underset{\displaystyle CH{=}CH_2}{\underset{|}{C}}HCH_2CH{=}CHCH_2CH_2OCH_3$$

1-Methoxy-6-β-methoxyethyloct-3,7-dien was formed as the only product of the direct action of metallic magnesium on the methoxychloropentenes. The structure of 1-methoxy-6-β-methoxyethyloct-3,7-dien was determined by its oxidation with potassium permanganate; formic and methoxypropionic acids were isolated and identified.

The formation of 1-methoxy-6-β-methoxyethyloct-3,7-dien and not 1,10-dimethoxydec-3,7-dien, as could be expected from a normal reaction of a primary methoxychloropentene with magnesium and an organo-magnesium compound, can be explained by means of an abnormal bimolecular mechanism proposed by the authors for an analogous type of reaction in a previous publication [2].

EXPERIMENTAL

Action of benzyl magnesium chloride on 1-methoxy-5-chloropent-3-en. An ether solution of benzyl magnesium chloride was prepared from 8 g of magnesium turnings and 42 g of benzyl chloride in 100 ml of absolute ether. 30 g of 1-methoxy-5-chloropent-3-en was added dropwise to this organo-magnesium compound, and the reaction mixture heated for 5 hours on the water bath. After cooling, it was treated with cold water and dilute hydrochloric acid. The ether layer was separated and dried with calcium chloride; the ether was removed and the residue vacuum distilled. After several redistillations, 8.9 g of 1-methoxy-3-benzylpent-4-ene, b.p. 111-113° at 11 mm, was obtained.

n_D^{20} 1.4860; d_4^{20} 0.9145; MR_D 59.65; calculated 59.81.

0.1216 g substance: 0.3647 g CO_2; 0.1017 g H_2O. Found %: C 81.85; H 9.36. $C_{13}H_{18}O$. Calculated %: C 82.00; H 9.47.

16.7 g of 1-methoxy-5-benzylpent-3-en, b.p. 123-124.5° at 10 mm, was also obtained.

n_D^{20} 1.5045; d_4^{20} 0.9336; MR_D 60.31; calculated 59.81.

0.1065 g substance: 0.3193 g CO_2; 0.0908 g H_2O. Found %: C 81.82; H 9.54. $C_{13}H_{18}O$. Calculated %: C 82.10; H 9.47.

In addition to the above, 6.3 g of dibenzyl, b.p. 132° at 100 mm, m.p. 52° was obtained.

Action of benzyl magnesium chloride on 1-methoxy-3-chloropent-4-en. An ether solution of benzyl magnesium chloride was prepared from 9.4 g of magnesium turnings and 53 g of benzyl chloride in 100 ml of absolute ether. 30 g of 1-methoxy-3-chloropent-4-en was slowly added dropwise to this solution, and the reaction mixture was then heated for 4 hours on a water bath. The reaction mixture was processed in the same manner as in the previous experiment. After several redistillations in vacuum the following were obtained: 7.6 g of 1-methoxy-3-benzylpent-4-en, b.p. 114-115° at 13 mm, n_D^{20} 1.4855; d_4^{20} 0.9153, 14.1 g 1-methoxy-5-benzylpent-3-en, b.p. 135-136° at 18 mm, n_D^{20} 1.5065, d_4^{20} 0.9346; and 8.1 g of dibenzyl, m.p. 51.5°.

Oxidation of 1-methoxy-5-benzylpent-3-ene with potassium permanganate. 45 g of potassium permanganate was added in portions with continuous stirring over a 4 hour period to 8 g of 1-methoxy-5-benzylpent-3-en in 350 ml of distilled water. The manganese dioxide precipitate was filtered and washed three times with hot distilled water. The aqueous solution of the salts was evaporated to a volume of 60 ml, and treated with dilute hydrochloric acid. The solution was extracted several times with ether and the ether extracts dried over $CaCl_2$. After removal of the ether, the residue was vacuum distilled. Three fractions were obtained (at 12 mm): 1) 106-113°, 1.9 g; 2) 114-140°, 0.5 g; 3) 140-146°, 2.5 g.

When the first fraction was redistilled, 1.1 g of methoxypropionic acid, b.p. 108-110° at 12 mm, n_D^{20} 1.4189 was isolated.

The third fraction solidified into a crystalline mass. Crystals of benzoic acid, m.p. 120-121°, were obtained on recrystallization from water.

Oxidation of 1-methoxy-3-benzylpent-4-en with potassium permanganate. 50 g of potassium permanganate was slowly added with thorough shaking to a flask containing 9 g of 1-methoxy-3-benzylpent-4-en. After decolorization of the liquid, the manganese dioxide was filtered and washed with hot distilled water. The water solution of the salts was evaporated to a volume of 65-70 ml, the salts decomposed with phosphoric acid, and the solution extracted four times with ether. The ether solution was dried with calcium chloride, the ether removed, and the residue distilled. Formic acid, b.p. 101-105°, n_D^{20} 1.3780; d_4^{20} 1.2210, was isolated; it had the sharp characteristic odor. A black precipitate of silver was obtained with a solution of ammoniacal silver oxide (on heating). After removal of the formic acid, the distillation flask was cooled. The crystalline mass which formed was recrystallized from water. White crystals of benzoic acid, m.p. 121°, were isolated.

Action of ethyl magnesium bromide on 1-methoxy-5-chloropent-3-en. 7.5 g of magnesium turnings were placed in a round-bottomed flask equipped with a reflux condenser and a dropping funnel. The magnesium turnings were activated by heating with a crystal of iodine, and on cooling, were covered with absolute ether. A solution of 35 g of ethyl bromide in 100 ml of absolute ether was then slowly added dropwise. The reaction mixture was heated for 1 hour on the water bath. 30 g of 1-methoxy-5-chloropent-3-en was then added dropwise to the organomagnesium compound, and the reaction mixture was heated for 2 hours on the water bath. At the end of the reaction, the mixture was treated with cold water and dilute hydrochloric acid. The ether layer was separated in a separatory funnel and dried over calcium chloride. After removal of the ether on the water bath, the residue was vacuum distilled. 3 fractions were obtained: 1) 53-60° at 30 mm, n_D^{20} 1.4198; 16.5 g; 2) 61-121° at 30 mm; n_D^{20} 1.4368; 1.1 g; 3) 113-118° at 16 mm; n_D^{20} 1.450; 4.8 g. 15.8 g of 1-methoxyhept-3-en, b.p. 58-59° at 30 mm, was obtained by redistilling the first fraction.

n_D^{20} 1.4200; d_4^{20} 0.8079; MR_D 40.09; calculated 40.32.

0.1106 g substance: 0.3030 g CO_2; 0.1243 g H_2O. Found %: C 74.76; H 12.58. $C_8H_{16}O$.
Calculated %: C 75.00; H 12.50.

4.2 g of 1-methoxy-6-β-methoxyethyloct-3,7-dien, b.p. 113-114° at 13 mm, was obtained by redistilling the third fraction.

n_D^{20} 1.4510; d_4^{20} 0.8846; MR_D 60.28; calculated 59.97.

0.1123 g substance: 0.2983 g CO_2; 0.1104 g H_2O. Found %: C 72.49; H 11.00. $C_{11}H_{20}O_2$.
Calculated %: C 72.72; H 11.11.

Action of ethyl magnesium bromide on 1-methoxy-3-chloropent-4-en. An ether solution of ethyl magnesium bromide was prepared from 9.1 g magnesium turnings and 43.1 g of ethyl bromide. 40 g of 1-methoxy-3-chloropent-4-en was then added dropwise to it, and the reaction mixture was heated for 1 hour on the water bath. The jelly-like mass which formed was treated with cold water and a cold solution of dilute hydrochloric acid. The ether layer was dried with calcium chloride, the ether was removed, and the residue vacuum distilled. After several redistillations, 23.5 g of 1-methoxyhept-3-en, b.p. 60-61° at 35 mm, n_D^{20} 1.4204; d_4^{20} 0.8080, and 6.7 g of 1-methoxy-6-β-methoxyethyloct-3,7-dien, b.p. 106-108° at 9 mm, n_D^{20} 1.4500; d_4^{20} 0.8850, were isolated.

Oxidation of 1-methoxyhept-3-en with potassium permanganate to the glycol. 100 ml of distilled water and 15 g of 1-methoxyhept-3-en were placed in a 5 liter flask. A weakly basic solution of 25 g of potassium permanganate in 2500 ml of water was slowly added dropwise with efficient mechanical stirring to the reaction mixture. The addition took 10 hours and the reaction mixture was then allowed to stand overnight. After the decolorization of the liquid, the manganese dioxide was filtered and washed several times with hot water. The filtrate was evaporated in vacuum to a volume of 40-50 ml, treated with hydrochloric acid, and extracted with ether. The ether extract was dried over sodium sulfate, the ether removed, and the residue vacuum distilled. 4.1 g of 1-methoxyhept-3,4-diol, b.p. 116-120° at 10 mm, resulted from the distillation.

n_D^{20} 1.4460; d_4^{20} 0.9950; MR_D 43.42; calculated 43.84.

0.1113 g substance: 0.2406 g CO_2; 0.1096 g H_2O. Found %: C 58.99; H 11.02. $C_8H_{16}O_2$.
Calculated %: C 59.25; H 11.11.

Oxidation of 1-methoxyhept-3-en with potassium permanganate to the acids. 10.5 g of 1-methoxyhept-3-en and 540 ml of water were placed in a one-liter flask. 30 g of potassium permanganate was slowly added with constant shaking, and the flask with the reaction mixture was left at room temperature for 12 hours. The manganese dioxide precipitate was filtered and washed several times with hot water. The filtrate was evaporated, in vacuum, to a volume of 50-60 ml, treated with hydrochloric acid, and extracted with ether. The ether extract was dried over calcium chloride, the ether removed, and the residue vacuum distilled. On distillation, 2.1 g of butyric acid, b.p. 160-162°, n_D^{20} 1.400; d_4^{20} 0.9680, and 2.5 g of methoxypropionic acid, b.p. 106-107° at 100 mm, n_D^{20} 1.4168, were obtained. (According to the literature methoxypropionic acid has a b.p. of 107-108° at 12 mm; n_D^{20} 1.4178).

Action of bromine on 1-methoxyhept-3-en. 10 g of bromine was added, with efficient stirring and cooling, (-15 to -18°) to 8 g of 1-methoxyhept-3-en. Upon distillation of the reaction mixture 11.2 g of 1-methoxy-3,4-dibromoheptane, b.p. 116-119° at 16 mm, was obtained.

n_D^{20} 1.4960; d_4^{20} 1.5055; MR_D 56.00; calculated 56.23.

0.1116 g substance: 0.1449 g AgBr. Found %: Br 55.20. $C_9H_{18}OBr_2$. Calculated %: Br 55.49.

Action of butyl magnesium bromide on 1-methoxy-5-chloropent-3-en. An ether solution of butyl magnesium bromide was prepared from 6.5 g of magnesium turnings and 38.7 g of butyl bromide. 30 g of 1-methoxy-5-chloropent-3-en was slowly added, dropwise with cooling, to it, and the reaction mixture was then heated for 3 hours on the water bath. At the end of the reaction, it was treated with water and dilute hydrochloric acid. After drying and removing the ether, the reaction mixture was twice vacuum distilled; 20.6 g of 1-methoxynon-3-en, b.p. 68-69° at 9 mm, was isolated.

d_4^{20} 0.8082; n_D^{20} 1.4295; MR_D 49.81; calculated 49.56.

0.1099 g substance: 0.3092 g CO_2; 0.1247 g H_2O. Found %: C 76.78; H 12.70. $C_{10}H_{20}O$. Calculated %: C 76.92; H 12.82.

2 g of 1-methoxy-6-β-methoxyethyloct-3,7-dien, b.p. 114-116° at 15 mm, n_D^{20} 1.4515; d_4^{20} 0.8841, was also obtained.

Action of butyl magnesium bromide on 1-methoxy-3-chloropent-4-en. An ether solution of butyl magnesium bromide was prepared from 10.3 g of magnesium turnings and 61.3 g of butyl bromide. 50 g of 1-methoxy-3-chloropent-4-en was added dropwise to the above solution. The reaction mixture was then heated for 2 hours on the water bath. The reaction mixture was then processed in a manner analogous to the previous experiment. Upon distillation of the reaction products 32.1 g of 1-methoxynon-3-en, b.p. 71-72° at 12 mm, n_D^{20} 1.4298; d_4^{20} 0.8075, and 6.1 g of 1-methoxy-6-β-methoxyethyloct-3,7-dien, b.p. 113-114° at 12 mm, n_D^{20} 1.4512; d_4^{20} 0.8840, was obtained.

Oxidation of 1-methoxynon-3-en with potassium permanganate to the glycol. 15 g of 1-methoxynon-3-en and 100 ml of distilled water were placed in a 2-liter flask. A weakly basic solution of 10.1 g of potassium permanganate in 1000 ml of water was then slowly added with efficient shaking. The addition took 6 hours. The reaction mixture was allowed to stand for 16 hours at room temperature. The manganese dioxide precipitate was filtered and washed with hot distilled water. The filtrate was evaporated to a volume of 50-60 ml, treated with dilute hydrochloric acid, and extracted with ether. The ether extract was dried over sodium sulfate, the ether removed, and the residue vacuum distilled. 3.1 g of 1-methoxynon-3,4-diol, b.p. 142-144° at 13 mm, was isolated.

n_D^{20} 1.4442; d_4^{20} 0.9782; MR_D 53.29; calculated 53.07.

0.1199 g substance: 0.2762 g CO_2; 0.1224 g H_2O. Found %: C 62.87; H 11.42. $C_{10}H_{22}O_2$. Calculated %: C 63.15; H 11.58.

Action of bromine on 1-methoxynon-3-en. 8.2 g of bromine was slowly added dropwise with cooling and stirring to 8 g of 1-methoxynon-3-en. The reaction product was distilled. 8.9 g of 1-methoxy-3,4-di bromopropane, b.p. 137-139° at 11 mm was isolated.

n_D^{20} 1.4920; d_4^{20} 1.4033; MR_D 65.32; calculated 65.47.

0.1165 g substance: 0.1379 g AgBr. Found %: Br 50.36. $C_{10}H_{20}OBr_2$. Calculated %: Br 50.50.

Action of magnesium on 1-methoxy-5-chloropent-3-en. 2.4 g of magnesium turnings were placed into a flask containing a stirrer, dropping funnel, and reflux condenser. The magnesium turnings were activated by heating with a crystal of iodine, and on cooling, were covered with absolute ether. A few drops of ethylbromide were then added followed by the slow dropwise addition of 30 g of 1-methoxy-5-chloropent-3-en. The reaction mixture was then heated for 5 hours with constant stirring. At the end of the reaction it was diluted with water,

and the ether layer separated and dried over calcium chloride. The ether was removed on the water bath and the residue vacuum distilled. On distillation, 15.7 g of 1-methoxy-5-chloropent-3-en was recovered, and 6.7 g of 1-methoxy-6-β-methoxyethyloct-3,7-dien, b.p. 111-112 at 10 mm, n_D^{20} 1.4515; d_4^{20} 0.8865, was isolated.

Action of magnesium on 1-methoxy-3-chloropent-4-en. An ether solution of 30 g of 1-methoxy-3-chloropent-4-en was added, dropwise, to 2.4 g of activated magnesium covered by a layer of absolute ether. The reaction mixture was then processed in the same way as the previous experiment. On distillation, 17.8 g of 1-methoxy-3-chloropent-4-en was recovered and 5.5 g of 1-methoxy-6-β-methoxyethyloct-3,7-dien b.p. 110-112° at 10 mm, n_D^{20} 1.4518; d_4^{20} 0.8855, was isolated.

Oxidation of 1-methoxy-6-β-methoxyethyloct-3,7-dien with potassium permanganate. 39.5 g of pulverized potassium permanganate was added, in small portions, with continuous stirring, to 15.5 g of 1-methoxy-6-β-methoxyethyloct-3,7-dien in 800 ml of distilled water in a 2 liter flask. After decolorization of the liquid, the manganese dioxide precipitate was filtered and washed several times with hot water. The filtrate was evaporated, treated with phosphoric acid, and extracted with ether. After removal of the ether, the residue was distilled. Formic acid, b.p. 101-106°, n_D^{20} 1.3770, sharp characteristic odor, was isolated. A black precipitate was formed (on heating) with an ammoniacal silver oxide solution. Methoxypropionic acid, b.p. 107-109° at 11 mm, n_D^{20} 1.4173, and a thick liquid fraction, b.p. 190-210° at 9 mm, were also obtained.

SUMMARY

1. The reactions of the isomeric methoxychloropentenes with benzyl magnesium chloride, ethyl magnesium bromide, and butyl magnesium bromide was studied.

2. Mixtures of isomeric methoxybenzylpentenes, identical in composition, were formed as a result of the reaction of benzyl magnesium chloride on the isomeric methoxychloropentenes.

3. Mixtures of the corresponding 1-methoxy-5-alkylpent-3-enes and 1-methoxy-6-β-methoxyethyloct-3,7-dien were obtained as a result of the action of ethyl magnesium bromide and butyl magnesium bromide on the isomeric methoxychloropentenes. The second compound was also obtained by the direct action of magnesium on the isomeric methoxychloropentenes.

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ALLYLIC REARRANGEMENTS

XVIII. REACTION OF ISOMERIC METHOXYCHLOROPENTENES WITH SALTS OF XANTHOGENIC ACIDS

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In a series of previous communications on the study of allylic rearrangements, the reactions of isomeric alkoxychloropentenes with various reagents was studied: alcoholic alkali, alkali metal acetates and alcoholates, sodium hydrosulfide, amines, sodio malonic ester, dialkyl phosphates, and organo-magnesium compounds. It was shown that with all of these, the reaction proceeds mainly according to two mechanisms – the bimolecular and the monomolecular. The reaction by means of the bimolecular mechanism has only one stage, is without rearrangements, and leads to compounds with structures analogous to the starting material. The reaction by means of the bimolecular mechanism has two stages: it proceeds by means of the initial formation of a carbonium ion and leads to the formation of either mixtures of isomeric compounds, or just one. In certain cases, a third mechanism is possible for the reaction – an abnormal bimolecular mechanism. This is of secondary importance as compared to the other two. The primary allylic chlorides, in comparison with the secondary, have a much more pronounced tendency to react by means of the bimolecular mechanism, which is related to peculiarities in their structure.

In order to further develop and increase the number of examples of reactions accompanied by allylic rearrangements, the preparation of xanthogenic esters from allylic halides was studied in this investigation.

The reaction between allylic halides and xanthogenic salts has remained almost uninvestigated up to now. Only allyl xanthogenates, obtained by the reaction of allyl bromide with xanthogenic salts [1], are reported in the literature; however, these publications do not give any bases for discussing the possibility of the occurrence of allylic rearrangements during these reactions. The study of the reaction of isomeric allylic halides with xanthogenic salts is also of considerable interest for gathering data to further develop the xanthogenic method of Chugaev for the preparation of unsaturated compounds.

The reactions of isomeric methoxychloropentenes with sodium ethyl- and butyl-xanthogenates was studied. The reaction was effected by heating in alcoholic solutions. Methoxypentenyl ethylxanthogenate and a series of lower boiling fractions were obtained in the experiments with primary methoxychloropentenes and sodium ethylxanthogenate.

$$CH_3OCH_2CH_2CH{=}CHCH_2Cl + C_2H_5OCSS^- \rightarrow CH_3OCH_2CH_2CH{=}CHCH_2SSCOC_2H_5 + Cl^-.$$

It is interesting to point out that methoxypentenyl ethylxanthogenate is obtained in pure form only when equimolecular or smaller amounts of sodium ethylxanthogenate than methoxychloropentene are used. When an excess of the sodium xanthogenate is used, a fraction is formed which has the same boiling point as methoxypentenyl ethylxanthogenate, but with much lower values for the constants and a much lower sulfur content. This occurrence, which seemed very strange at first, was explained when the reaction between sodium ethylxanthogenate and a secondary methoxychloropentene, 1-methoxy-3-chloropent-4-en, was studied. Dimethoxypentenyl thioether $(CH_3OCH_2CH_2CH{=}CHCH_2)_2S$ was obtained as the main product along with a series of lower boiling products.

The thioether, according to its constants, corresponded closely to the one obtained by one of the authors and N. N. Kudryavtseva, by the action of sodium hydrosulfide on the isomeric methoxychloropentenes [2]. It was shown that the primary methoxypentenyl mercaptan, formed from both of the isomeric methoxychloropentenes as main products, was transformed, under these reaction conditions (heating in alcohol), into the corresponding thioether by the elimination of a molecule of hydrogen sulfide. According to the constants, both of the isomeric methoxychloropentenes formed the identical thioether. The structure of the mercaptan and the thioethers was determined by oxidizing them with potassium permanganate.

The formation of methoxypentenyl thioether, by the reaction of secondary methoxychloropentenes with sodium ethylxanthogenate can be explained in the following manner: the secondary methoxychloropentene reacts monomolecularly with sodium ethylxanthogenate, in the first stage of the reaction, with complete allylic rearrangement to form methoxypentenyl ethylxanthogenate; however, this reaction occurs at a considerably slower rate in comparison to the analogous reaction of the methoxychloropentene, because its rate is limited by the slow formation of ions from the secondary methoxychloropentene by the action of the solvent; as a result, the methoxypentenyl ester which has already been formed, is in contact, for long periods of time with the yet unreacted xanthogenate and evidently, with the sodium ethylate present in the medium, and decomposes to form the mercaptan [1]; the latter, under these reaction conditions (heating in alcohol) is transformed, as shown previously [2], into the thioether by the elimination of hydrogen sulfide.

The abnormal behavior of the secondary methoxychloropentene in this reaction is not unusual, as this behavior was noted frequently in other reactions. For example, when it was reacted with sodio alkylacetoacetic ester, the methoxypentenyl alkyl acetoacetic ester formed in the first stage of the reaction is decomposed by the action of the alcoholate and the sodio alkyl acetoacetic ester into disubstituted derivatives of acetic acid [3]; on reaction with dialkyl phosphate salts, an addition of a second molecule of sodium dialkylphosphate occurs at the double bond of the methoxypentenyl phosphoric ester formed in the first stage of the reaction [4].

In the light of the many reactions with secondary methoxychloropentenes conducted for determination of the reaction mechanism the results obtained from the reaction of primary methoxychloropentenes with xanthogenates, which seem so strange at first, become quite understandable. As was previously mentioned, methoxypentenyl ethylxanthogenate can only be obtained in pure form in the absence of an excess of the sodium xanthogenate in the reaction medium. In the presence of the latter, a complete decomposition of the ester to methoxypentenylmercaptan followed by its transformation to the thioether occurs. The boiling points of methoxypentenyl ethylxanthogenate and methoxypentenyl ether are so close that they cannot be separated by distillation; they can be distinguished by differences in the refractive indices, densities and especially by the sulfur content, which differs considerably. The variation of the constants and the amount of sulfur in the main fractions of the xanthogenic ester obtained in the series of experiments with excesses of the xanthogenate, can be explained by the presence of distinguishable amounts of thioether. Results analogous to those reported above for the reaction with ethylxanthogenate were obtained for the reaction between the isomeric methoxychloropentenes and sodium butylxanthogenate. Methoxypentenyl butylxanthogenate resulted from the action of sodium butylxanthogenate on 1-methoxy-5-chloropent-3-en, and dimethoxypentenyl thioether from the analogous reaction with 1-methoxy-3-chloropent-4-en.

EXPERIMENTAL

Action of sodium ethylxanthogenate on 1-methoxy-5-chloropent-3-en. 23 g of carbon disulfide was slowly added, dropwise with cooling, to a solution of sodium ethylate prepared from 6.3 g of metallic sodium and 100 ml absolute ethanol. 40 g of 1-methoxy-5-chloropent-3-en was then added, in the cold, to the alcoholic solution of sodium ethylxanthogenate. Very rapid precipitation of sodium chloride occurred. The reaction mixture was heated for 2 hours on the water bath. After filtration of the sodium chloride precipitate and removal of the alcohol, the residue was vacuum distilled. After two distillations, in addition to fractions boiling at 66-124° at 10 mm, 23.3 g of methoxypentenyl ethylxanthogenate, b.p. 161-162 at 12 mm, was isolated.

n_D^{20} 1.5315; d_4^{20} 1.0676.

0.7181 g substance: 0.3684 g $BaSO_4$. Found %: S 29.08. $C_8H_{16}O_2S_2$. Calculated %: S 29.09.

Action of sodium butylxanthogenate on 1-methoxy-5-chloropent-3-en. An alcoholic solution of sodium butylxanthogenate was prepared from 16 g of carbon disulfide, 3.2 g of sodium, and 80 ml of absolute butyl alcohol. 20 g of 1-methoxy-5-chloropent-3-en was then slowly added dropwise to the alcoholic solution of the sodium xanthogenate. A very rapid precipitation of sodium chloride occurred. After the addition of the chloride, the reaction mixture was heated for 2 hours on the water bath. The sodium chloride precipitate was filtered, the butyl alcohol was removed in a slight vacuum, and the residue was vacuum distilled. 18.9 g of methoxypentenyl butylxanthogenate, b.p. 170-170.8° at 10 mm, was obtained.

n_D^{20} 1.5220; d_4^{20} 1.0400.

0.1286 g substance: 0.2402 g $BaSO_4$. Found %: S 25.66. $C_{11}H_{20}O_2S_2$. Calculated %: S 25.72.

Action of sodium ethylxanthogenate on 1-methoxy-3-chloropent-4-en. 14.3 g of carbon disulfide was slowly added, dropwise, with ice cooling, to a solution of sodium ethylate prepared from 3.9 g of metallic sodium and 50 ml of absolute ethyl alcohol. 20 g of 1-methoxy-3-chloropent-4-en was then added, and the reaction mixture was heated for two hours on the water bath. The sodium chloride precipitated much more slowly than during the analogous reaction with 1-methoxy-5-chloropent-3-en.

At the end of the heating, the sodium chloride precipitate was filtered, the ethyl alcohol was removed on the water bath, and the residue was vacuum distilled. After two distillations, in addition to fractions boiling at 84-144° at 10 mm, 5.24 g of di-methoxypentenyl thioether, b.p. 161-163° at 11 mm, was obtained.

n_D^{20} 1.4943; d_4^{20} 0.9786.

0.1272 g substance: 0.1458 g $BaSO_4$. Found %: S 14.01. $C_{12}H_{22}O_2S$. Calculated %: S 13.90.

Action of sodium butylxanthogenate on 1-methoxy-3-chloropent-4-en. A solution of sodium butylate in absolute butyl alcohol was prepared from 6.9 g of metallic sodium and 200 ml of butyl alcohol. 28 g of carbon disulfide was then added, dropwise with cooling, followed by 40 g of 1-methoxy-3-chloropent-4-en. The reaction mixture was heated for 3 hours on the water bath. After separation of the sodium chloride and removal of the butyl alcohol, the residue was vacuum distilled. After two distillations, 15.9 g of dimethoxypentenyl thioether, b.p. 157-159° at 8 mm, n_D^{20} 1.4935; d_4^{20} 0.9758, and a series of lower boiling fractions were obtained.

SUMMARY

1. The reaction between the isomeric methoxychloropentenes and sodium ethyl and butylxanthogenate was studied.

2. 1-Methoxy-5-chloropent-3-en reacted normally with sodium ethyl- and butylxanthogenate to form 1-methoxypentenyl ethyl- and butylxanthogenate.

3. Dimethoxypentenyl thioether was formed as the main product of the reaction between sodium ethyl- and butylxanthogenate with 1-methoxy-3-chloropent-4-en. The reaction occurred with a complete allylic rearrangement. A mechanism for the formation of dimethoxypentenyl thioether is given.

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A STUDY OF THE TRANSFORMATIONS OF PINACONES WITH SUBSTITUTED ACETYLENIC RADICALS

IX. SYNTHESIS AND TRANSFORMATIONS OF TRIPHENYLPHENYL-ACETYLENYL ETHYLENE GLYCOL (1,1,2,4-TETRAPHENYLBUTYN-3-DIOL-1,2)

E. D. Venus-Danilova and V. I. Serkova

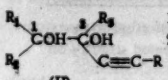
In a previous communication [1] the transformations of trimethylphenylacetylenylethylene glycol (2,3-dimethyl-5-phenylpentyne-4-diol-2,3) by the action of 30% sulfuric acid were discussed.

An acetylenic ketone, dimethylphenylacetylenylacetylmethane, as well as the decomposition products of an ethylenic γ-ketol, a dienic ketone and a mixture of ethylideneacetophenone and acetone, were found in the transformation products of this glycol.

The formation of these products shows that trimethylphenylacetylenylethylene glycol undergoes both a pinacoline and an acetylene-allene rearrangement at the same time, similar to the previously studied compounds, symmetrical methyldiphenylphenylacetylenylethylene glycol [2], methyldiphenyltertiarybutylacetylenylethylene glycol [3], and trimethylphenylacetylenyl glycol [1].

In order to continue the study of the effects of the substituents of the hydroxyl-containing carbon atoms of the acetylenic tertiary γ-glycols [4,5,6,7,1,2,3] on their transformations, as well as to elucidate the mechanism [8] of this transformation and to study the properties of ethylenic γ-ketols, the eighth member of this series, triphenylphenylacetylenylethylene glycol (1,1,2,4-tetraphenylbutyn-3-diol-1,2) [1] was synthesized and subjected to the action of sulfuric acid under the previously described conditions.

From the previous study it was concluded that the presence of two phenyl groups on the first hydroxyl-containing carbon atom of the glycol (II) favors the pinacoline rearrangement; a methyl group on the second hydroxyl-group-containing atom has the analogous effect.



(II)

1. Pinacoline rearrangement (dehydration) $R_1 = R_2 = C_6H_5$, $R_3 = CH_3$
2. Acetylene-allene rearrangement (isomerization) $R_1 = R_2 = CH_3$, $R_3 = C_6H_5$

The opposite arrangement of the groups, the methyl groups on the first carbon atom and the phenyl groups on the second, favors the acetylene-allene rearrangement.

The structure of the triphenylphenylacetylenylethylene glycol is such that both transformations are probable: 1) the pinacoline rearrangement because of the presence of the phenyl groups on the first carbon atom, and 2) the acetylene-allene rearrangement, because of the phenyl group on the second carbon atom of the glycol.

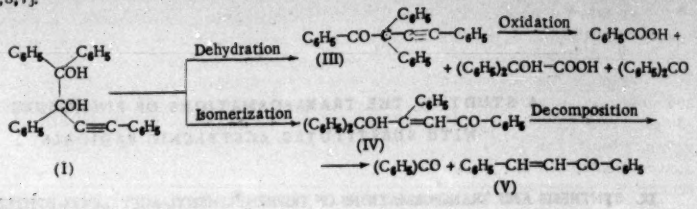
The experimental results proved this hypothesis to be true.

Triphenylphenylacetylenylethylene glycol (I) was obtained as coarse crystals, m.p. 114-115°, by the action of phenylbenzoin upon phenylacetylenyl magnesium bromide (Iotsich method) in a 53% yield based on the quantity of phenylbenzoin used.

As a result of the action of 30% sulfuric acid on triphenylphenylacetylenylethylene glycol, two products were isolated: a crystalline substance, m.p. 186-187°, and an oily liquid.

Upon the oxidation of the crystalline substance, benzoin, benzilic acid, and benzophenone were obtained. The structure of the ketone obtained, is, therefore, diphenylphenylacetylenylbenzoylmethane (1,2,2,4-tetraphenylbutyne-3-one-1)(III). In this case the ketone is formed by the removal of the mobile hydroxyl group in the α-position

to the triple bond [1,2,3,7].



A study of the oily liquid showed that the substance contained a double bond and a carbonyl group. A distillation at reduced pressure did not produce any homogeneous substance with a narrow boiling point. This fraction was shown to be a mixture of benzophenone and benzalacetophenone (V) by a molecular weight determination and by an oxidation of the substance. The above was confirmed by the formation of semicarbazones and by the pyrazoline reaction.

Benzophenone and benzalacetophenone, apparently, result from a ketonic cleavage of the extremely unstable ethylenic γ-ketol [1,1,2,4-tetraphenylbutyne-2-ol-1-one-4) [IV] which probably decomposed before distillation either by the action of the sulfuric acid or on washing the ether solution with the dilute aqueous sodium carbonate.

This conclusion was verified by the decreased molecular weight of the oily liquid and by its oxidation products (benzoic acid, benzoylformic acid, and benzophenone) before vacuum distillation. The instability of ethylenic γ-ketols of analogous structure and their ketonic cleavage was discovered previously [1,2].

On heating triphenylphenylacetylenylethylene glycol with 35% sulfuric acid, a slight fluorescence was detected in the acidic solution, which indicated that a small amount of an oxonium salt of a substituted dihydrofuran was present. However, after the separation of the transformation products of the glycol – the acetylenic ketone, benzalacetophenone, and benzophenone – only traces of a crystalline substance giving a fluorescence in strong sulfuric acid were isolated by ether extraction. This substance was not investigated further because of the small amount isolated.

Therefore, triphenylphenylacetylenylethylene glycol, on treatment with 30 and 35% sulfuric acid, forms the products of the pinacoline and the acetylene-allene rearrangements. The acetylenic ketone is obtained from the dehydration of the glycol and, on isomerization, the glycol forms the unstable ethylenic γ-ketol which splits, as soon as it is formed, into benzophenone, and benzalacetophenone.

EXPERIMENTAL

1. The Synthesis of Triphenylphenylacetylenylethylene Glycol (1,1,2,4-Tetraphenylbutyne-3-Diol-1,2).

An ether solution of 7.6 g of phenylacetylene was added to a freshly prepared solution of ethyl magnesium bromide made from 1.8 g of magnesium and 8 g of ethyl bromide. The reaction mixture was heated slightly on the water bath until the evolution of ethane ceased.

A solution of 10 g of phenylbenzoin (m.p. 86-87°) was added to the above Grignard with stirring and cooling with ice. After the addition of all of the phenylbenzophenone, the contents of the flask were heated to a slight reflux of the ether.

After three days the reaction mixture was decomposed with ice and water, acidified with dilute sulfuric acid, and extracted with ether. The ether extracts were washed with aqueous sodium carbonate, then with water, and dried with fused sodium sulfate. After the removal of the ether, the thick residual mass quickly began to crystallize. After recrystallization from a mixture of petroleum ether and ether, 8.5 g of a substance, coarse crystals, m.p. 114-115°, was obtained. The yield was 74 % of the theoretical, calculated on the amount of phenylbenzoin used.

Three runs using this synthesis produced 28.8 g of the glycol with an average yield of 61% of the theoretical.

0.1096 g substance: 0.3449 g CO_2; 0.0587 g H_2O. 0.1322 g substance: 0.4159 g CO_2; 0.0678 g H_2O. Found %: C 85.82, 85.80; H 5.95, 5.69. $C_{28}H_{22}O_2$. Calculated %: C 86.15; H 5.67. 0.2216 g substance: 20.50 g C_6H_6: Δt 0.14°. Found: M 386. $C_{28}H_{22}O_2$. Calculated M: 390.

The number of hydroxyl groups was determined according to Terentyev.

0.0695 g substance: 8.2 ml CH_4 (14°, 751.5 mm). Found v_0 7.6 ml; % OH 7.9. $C_{28}H_{26}(OH)_2$. Calculated v_0 8.5 ml; % OH 8.7.

II. The Action of Sulfuric Acid on Triphenylphenylacetylenylethylene Glycol.

Expt. 1. The action of 30% sulfuric acid. 8 g of the glycol, m.p. 114-115°, was heated with 80 ml of 30% sulfuric acid to a gentle boil for 3 hours with good stirring. The glycol melted and formed a yellow mass; no fluorescence could be observed in the solution. The ether extract of the acidic solution was washed with aqueous sodium carbonate and then with water. After the removal of the ether, 7.3 g of a thick, light-yellow liquid which upon standing gave 0.8 g of a crystalline substance, m.p. 185-187°, was obtained. After recrystallization from a boiling mixture of ether and petroleum ether, the crystals melted at 186-187°.

The liquid from which the crystalline substance separated, was unsaturated in character (tests with aqueous potassium permanganate and bromine in chloroform).

Nothing could be isolated from the ether extracts of the neutralized solution.

Expt. 2. The action of 35% sulfuric acid. 7 g of the glycol was mixed with ten parts by weight of 35% sulfuric acid and the solution boiled gently for three hours.

On cooling, a thick, sticky, dark-brown liquid layer containing dispersed crystals separated. The lower aqueous acidic layer had a barely detectable, greenish-yellow fluorescence.

6.2 g of a thick yellow liquid, from which 0.5 g of crystals, m.p. 185-187° (analogous to those obtained in the first experiment) separated on standing, was obtained from the ether extracts.

The ether extracts of the neutralized solution (the fluorescence disappeared when the solution was neutralized with aqueous sodium carbonate) gave an insignificant amount of a solid substance showing a fluorescence in strong sulfuric acid. The substance was not investigated further because of its small quantity.

III. The Substance With M.P. of 186-187° Obtained from the Acidic Solution.

The substance is soluble in benzene and pyridine, and slightly in ether. It does not give methane with methyl magnesium iodide. It decolorizes a solution of bromine in chloroform and aqueous potassium permanganate.

0.0966 g substance: 0.3187 g CO_2; 0.0460 g H_2O. 0.0800 g substance: 0.2641 g CO_2; 0.0374 g H_2O. Found %: C 89.98, 90.04; H 5.29, 5.19. $C_{28}H_{20}O$. Calculated %: C 90.32; H 5.37. 0.2230 g substance: 31.0 g C_6H_6: Δt 0.10°. Found: M 359. $C_{28}H_{20}O$. Calculated: M 372.

From these results it can be concluded that this substance is an acetylenic ketone obtained by the dehydration of triphenylphenylacetylenylethylene glycol. However, as with the previously studied phenylphenylacetylenylbenzoylmethane [7], the semicarbazone could not be obtained. The yield of the ketone was 0.8 g, 10.5% of the theoretical.

In order to establish the structure of the ketone, it was oxidized with potassium permanganate in pyridine.

Oxidation of the ketone with m.p. of 186-187°. For the oxidation 1 g of the ketone dissolved in 50 ml of pyridine, and 50 ml of 2% aqueous potassium permanganate were used. The last 0.6 g of the potassium permanganate was added in small portions to correspond with the decolorization of the solution. The oxidation was run over a five hour period, at first, in the cold, and at the end heated to 40°. After decolorization of the solution, the manganese dioxide was filtered off and washed with hot water. Pyridine and other steam-volatile substances were removed from the filtrate by heating it in a slight vacuum. The pyridine in the distillate was neutralized with the calculated amount of sulfuric acid and an ether extraction was made. Benzophenone was obtained from the ether extracts and characterized by its melting point and by its semicarbazone, m.p. 164°, which gave no depression in melting point when mixed with authentic benzophenone semicarbazone. Benzophenone was also separated from the neutral steam-distillable products.

Dilute sulfuric acid was used to liberate the acids from the concentrated solution of their salts after the neutral substances were steam-distilled. A copious amount of benzoic acid, m.p. 120°, separated. After separation of the benzoic acid, the filtrate was extracted with ether to give a small amount of a crystalline substance which gave a red color characteristic for benzilic acid [9] with strong sulfuric acid. No other acids could be found in the oxidation products of the ketone.

Therefore, on the basis of the oxidation products—benzoic acid, benzilic acid, and benzophenone (a

product of the further oxidation of benzilic acid), the structure diphenylphenylacetylenylbenzoylmethane [1,2,2,4-tetraphenylbutyne-3-one-1) [III] can be assigned to the ketone obtained.

IV. Investigation of the Liquid From the Acidic Solution.

The liquid readily decolorizes aqueous potassium permanganate and bromine water. It does not give a qualitative test for the presence of a hydroxyl group. It forms a semicarbazone, m.p. 156-159°. It reacts with phenylhydrazine to form a polycrystalline mass which shows a strong pyrazoline reaction.

When the substance was vacuum distilled at 3 mm, a fraction, b.p. 130-145°, was obtained. A molecular-weight determination and an oxidation of this substance showed that it was not homogeneous.

0.1340 g substance; 16.96 g C_6H_6; Δt 0.23°. Found: M 174. $C_{13}H_{10}O$ (benzophenone). Calculated: M 182. $C_{15}H_{12}O$ (benzalacetophenone). Calculated: M 208. $C_{28}H_{22}O_2$ (ethylidene γ-ketol). Calculated: M 390.

Oxidation of the fraction with b.p. 130-145°, at 3 mm.

50 ml of a 2% aqueous solution of potassium permanganate was added to a solution of 1 g of the liquid in 20 ml of pyridine. The remaining 1 g of the oxidizing agent was added in small portions to correspond with the decolorization of the solution. The oxidation was conducted at 30-35° for a 3-hour period with thorough mixing.

After removal of the pyridine in the usual manner, benzophenone, m.p. 47°, giving a semicarbazone with m.p. 164° was isolated from the neutral products. Benzoic acid, m.p. 120°, was obtained by the splitting of the salts of the organic acids. After the removal of the benzoic acid, the aqueous solution, on mixing with phenylhydrazine hydrochloride, gave a yellow flocculent substance, m.p. 151°. According to the literature, the reaction product of benzoylformic acid and phenylhydrazine melts at 153° [10].

Therefore, the isolation of benzophenone, benzoic acid, and benzoylformic acid shows that the liquid is a mixture of benzophenone and benzalacetophenone, the products of the ketonic cleavage of the unstable γ-ketol-1,1,2,4-tetraphenylbutyne-2-ol-1-one-4.

Distillation of the mixture of benzophenone and benzalacetophenone did not separate them because of the closeness of their boiling points (b.p. of benzophenone 305° [11], b.p. of benzalacetophenone 348° [12]. The semicarbazones of these substances also have similar melting points (benzophenone semicarbazone, m.p. 164° [12], benzalacetophenone semicarbazone, m.p. 168° [13]. The semicarbazone of the substance melts at 156-159° and is apparently a mixture of the two semicarbazones. It was found impossible to separate this mixture into the two individual components because of their similar solubility in the common solvents.

In order to answer the question when does the cleavage of the ethylenic γ-ketol take place, during its distillation or at the moment of its formation, the liquid product isolated from the acid solution of the transformation products of the pinacol was analyzed immediately after the distillation of the ether without vacuum distilling it.

Its molecular weight was found to be between 215-218. The molecular weight of benzophenone is 182, that of benzalacetophenone is 208, and that of the unsaturated γ-ketol, 390.

The same products, benzophenone, benzoic acid, benzoylformic acid were isolated from the reaction with aqueous potassium permanganate as from the previous oxidation. Pure semicarbazones and pyrazolines could not be obtained in this case because mixtures were formed.

SUMMARY

1. A new acetylenic pinacol (triphenylphenylacetylenylethylene glycol) was synthesized and its transformation in 30 and 35 % sulfuric acid studied.

2. It was shown that the pinacol rearranged in two ways: an acetylenic ketone, diphenylphenylacetylenylbenzoylmethane (1,1,2,4-tetraphenylbutyne-3-one-1) was formed by a pinacoline rearrangement, and an unstable ethylenic γ-ketol as a result of an acetylene-allene rearrangement.

3. It was proven that a phenyl group on the first hydroxylated carbon atom favors the pinacoline rearrangement (the formation of the acetylenic ketone), and the presence of a phenyl group on the second carbon atom, the acetylene-allene rearrangement (the formation of the ethylenic γ-ketol).

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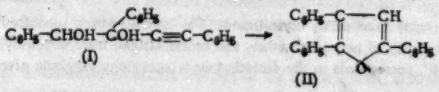
TRANSFORMATIONS OF SECONDARY-TERTIARY ACETYLENIC α-GLYCOLS PRODUCED BY MERCURY SALTS

II. 3-METHYL-5-PHENYL-PENTYN-4-DIOL-2,3

E. D. Venus-Danilova and V. M. Albitzkaya

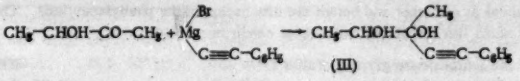
In a previous communication [1], it was shown that the acetylenic secondary-tertiary glycol, diphenylphenylacetylenylethylene glycol (I) (1,2,4-triphenyl-butyn-3-diol-1,2) was transformed into 2,3,5-triphenylpyran (II) by the action of an alcoholic solution of mercuric chloride.



(I) (II)

In order to see if this transformation was characteristic of other secondary-tertiary acetylenic glycols, the action of mercuric chloride upon 3-methyl-5-phenylpentyn-4-diol-2,3 (dimethyl-phenylacetylenylethylene glycol)(III) was studied under the analogous conditions.

Dimethylphenylacetylenylethylene glycol was obtained by the method of Iotsich from methylacetylcarbinol and phenylacetylenyl magnesium bromide.



(III)

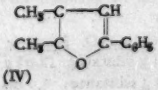
The glycol was obtained in two isomeric forms; one, m.p. 104-105°, was obtained as a first crop from a thick syrupy liquid, the other, m.p. 54-55°, separated after the mother liquor from the higher melting form was diluted with petroleum ether.

The higher melting (104-105°) modification of dimethylphenylacetylenylethylene glycol is reported in the literature [2], by F. Ya. Perveev, who synthesized it by hydrolyzing the corresponding α-oxide in very dilute hydrochloric acid.

Other cases where γ-glycols are formed in two or even three modifications, were reported by Du Pont [3] for tetramethylbutyndiol, and by A. L Lebedeva and R. P. Riskina [4] for symmetrical dimethyl-di-p-tolylbutyndiol.

The two isomeric dimethylphenylacetylenylethylene glycols obtained are differentiated by different melting points, and by different rates of crystallization from dilute alcohol. Because of the presence of two assymmetric carbon atoms in the dimethylphenylacetylenylethylene glycol, four optical isomers and two racemic compounds are possible.

Only one product, 2,3-dimethyl-5-phenylfuran (IV) was obtained in identical yields (average 69 %) by the action of an alcoholic solution of mercuric chloride upon both forms of the glycol.



(IV)

The structure of the substance, b.p. of 108-112°, as a substitued furan, was proven by analysis and by the

formation of a maleic anhydride addition product, m.p. 194-195°.

The literature [5] gives an analogous boiling point for 2,3-dimethyl-5-phenylfuran and a m.p. of 195° for its maleic anhydride addition product.

It therefore follows, that dimethylphenylacetylenylethylene glycol (II) resembles diphenylphenylacetylenylethylene glycol (I) [1] in dehydrating and cyclyzing to a trisubstituted furan by the action of an alcoholic solution of mercuric chloride.

EXPERIMENTAL

I. The Synthesis of 3-Methyl-5-phenylpentyn-4-diol-2,5.

8 g of magnesium, 36 g of ethyl bromide, 34 g of phenylacetylene, and 14 g of freshly distilled methylacetylcarbinol were used in the synthesis.

The methylacetylcarbinol, in three volumes of dry ether, was added over a 2 hour period with strong mixing to the phenylacetylenyl magnesium bromide and the reaction mixture warmed slightly at the end of the reaction (25-35°). After 2 days, the resulting yellow brown thick mass was decomposed with ice and a solution of ammonium chloride, and extracted with ether. The ether extracts were dried with sodium sulfate. After removal of the ether, the phenylacetylene was distilled off at 12 mm, and 28-30°.

After 24 hours the thick syrupy mass partly crystallized. The crystals which separated were filtered on a glass filter, washed with a small quantity of petroleum ether, and recrystallized from 40% ethyl alcohol. The white crystalline substance, m.p. 104-105°, corresponds to the dimethylphenylacetylenylethylene glycol reported in the literature [2].

The syrupy mother liquor, after addition of the petroleum ether during the washing of the crystals, m.p. 104-105°, also crystallized on standing. The crystals were separated on a glass filter and recrystallized several times from40% aqueous ethyl alcohol until a constant melting point 54-55° was obtained.

Four runs were made under analogous conditions. The only modification was the cooling of the reaction mixture with water during the addition of the methylacetylcarbinol. The crystalline substance, m.p. 104-105°, separated after the removal of the ether and before the distillation of the phenylacetylene. The crystalline products obtained were much less discolored under these conditions.

The results of the synthesis are given in Table 1.

TABLE 1

Expt. No.	Quantities				Yield of the glycol				Total yield
	Magnesium (in g)	Ethyl bromide (in g)	Phenylacetylene (in g)	Methylacetylcarbinol (in g)	M.p. 105°		M.p. 55°		
					in g	in %	in g	in %	
1	8	36	34	14	8	26.7	3.5	11.7	38.4
2	8	36	34	14	3.5	11.6	10	33.3	44.9
3	6.8	31	29	12	—	—	15	57.7	57.7
4	6	27	25.5	10.6	—	—	12	52.7	52.7
	28.8	130	122.5	50.6	11.5	9.6	40.5	38.9	48.5

The total yield of 48.5% of the glycol is calculated on the basis of the methylacetylcarbinol used.

After several recrystallizations from petroleum ether and finally from aqueous alcohol, 9 g of the glycol, with m.p. 105°, and 27.5 g of the glycol with m.p. 55° were obtained.

Both of the products are readily soluble in ether, benzene, chloroform, and alcohol; they are poorly soluble in petroleum ether. In this solvent and in aqueous alcohol, the higher melting form is somewhat more insoluble than the lower melting form. Both forms decolorize a solution of bromine in chloroform and aqueous potassium permanganate.

Analysis of the substance with m.p. 105°.
0.1471 g substance: 0.4047 g CO_2; 0.1030 g H_2O. Found %: C 75.05; H 7.80. $C_{12}H_{14}O_2$. Calculated %: C 75.79; H 7.36. 0.1894 g substance; 15.07 g C_6H_6: Δt 0.34°. Found: M 185. $C_{12}H_{14}O_2$. Calculated: M 190. 0.0164 g substance: 4.0 ml CH_4 (16°, 758.1 mm). Found: v_0 3.7 ml; % OH 17.30. $C_{11}H_{12}(OH)_2$. Calculated: v_0 3.8 ml; % OH 17.89.

2. Analysis of the substance with m.p. 55°.

0.1092 g substance: 0.3024 g CO_2; 0.0704 g H_2O. Found %: C 75.52; H 7.53. $C_{12}H_{14}O_2$. Calculated %: C 75.79; H 7.36. 0.1199 g substance; 13.68 g C_6H_6: Δt 0.23°. Found: M 187. $C_{12}H_{14}O_2$. Calculated: M 190. 0.0332 g substance: 8.5 ml CH_4 (20°, 759 mm). Found: v_0 7.7 ml; % OH 17.70. $C_{12}H_{13}(OH)_2$. Calculated: v_0 7.9 ml; % OH 17.89.

Fusion of the substance with m.p. 55° with potassium carbonate [6]. A mixture of 0.5 g of the substance and 0.28 g of potassium carbonate was heated on an oil bath in a flask containing an outlet tube. The substance began to decompose at a temperature of 190-195°. The decomposition products were introduced into an ammoniacal silver oxide solution, whereupon a copious white, flocculant precipitate of silver phenylacetylide formed.

On the basis of the analytical results, it can be seen that, when dimethylphenylacetylenylethylene glycol is synthesized by the method of Iotsich, a mixture of two isomers of this glycol are obtained in which the lower melting form predominates.

II. The Action of Mercuric Chloride on Dimethylphenylacetylenylethylene Glycol

Experiment 1. 0.4 g of mercuric chloride was added to a saturated alcoholic solution of 2 g, of the glycol with m.p. 105°, and the mixture heated on a boiling water bath for 8 hours in a closed tube. After this, the alcohol was distilled off. The residual greenish liquid was washed several times with water, extracted with petroleum ether, and dried with sodium sulfate. After removal of the ether, the reaction product was distilled at 4 mm, where it boiled at 108-112°.

Experiment 2. A saturated alcoholic solution of 2 g of the glycol, with m.p. 55° and 0.5 g of mercuric chloride were heated for 8 hours on a boiling water bath. The reaction products were isolated in the same manner as in Experiment 1. The product obtained also boiled at 108-112° at 4 mm.

The results of five experiments are given in Table 2. The duration of heating was 8 hours for all of the experiments.

TABLE 2

Expt. No.	Quantity			Yield of substance with b.p. 108-112° at 4 mm	
	$HgCl_2$ (in g)	Glycol with m.p. 105° (in g)	Glycol with m.p. 55° (in g)	(in g)	(in %)
1	0.3	1	–	0.6	66.7
2	0.5	–	2	1.2	66.7
3	0.5	–	2	1.2	66.7
4	0.4	2	–	1.3	72.2
5	0.8	–	4	2.5	69
	2.5	3	8	6.8	68

The substance, with b.p. 108-112° at 4 mm, when freshly distilled, is a clear, very slightly greenish liquid, which rapidly darkens on exposure to air. It decolorizes aqueous potassium permanganate and a solution of bromine in chloroform. It does not give a reaction for a carbonyl or a hydroxyl group. Strong sulfuric acid changes the substance into a brown, tarry liquid. A pine splinter moistened with hydrochloric acid is colored dark green by the vapors of the substance.

0.0921 g substance: 0.2814 g CO_2; 0.0617 g H_2O. Found %: C 83.37; H 7.38. $C_{12}H_{12}O$. Calculated %: C 83.72; H 6.99. 0.1613 g substance; 17.81 g C_6H_6: Δt 0.28°. Found: M 165. $C_{12}H_{12}O$. Calculated: M 172.

d_0^0 1.0094; d_{20}^{20} 1.0070; d_4^{20} 1.0092; n_D^{20} 1.58670. Found: MR_D 55.02. $C_{12}H_{12}O$. Calculated: MR_D 55.26.

The product of condensation with maleic anhydride was obtained by reacting 1.15 g of the substance, with b.p. 108-112° at 4 mm, with 0.86 g of maleic anhydride in anhydrous ether. After 16 days, the coarse, clear, prismatic crystals, m.p. 193-195°, described in the literature for the maleic anhydride addition product of 2,3-dimethyl-5-phenylfuran [5] were obtained.

On the basis of the analysis and the chemical properties of the product obtained, it can be considered that dimethylphenylacetylenylethylene glycol is transformed into 2,3-dimethyl-5-phenylfuran by the action of mercuric chloride in an average yield of 68%.

SUMMARY

1. When 3-methyl-5-phenylpentyn-4-diol-2,3 (dimethylphenylacetylenylethylene glycol) is synthesized by means of an organo-magnesium compound, two forms of the glycol are obtained: a higher melting form, m.p. 105°; and a lower melting form, m.p. 55°.

2. It was shown that both forms give 2,3-dimethyl-5-phenylfuran in identical yields by the action of mercuric chloride.

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COMPOUNDS CONTAINING A THREE-MEMBERED OXIDE RING

I. REACTION OF ETHYL β,β'-DIMETHYLGLYCIDATE WITH AMMONIA

S. N. Danilov and V. F. Martynov

The glycidic acids, as a new class of organic compounds, were discovered in 1880 by P. G. Melikov [1]. He obtained the simplest member of this class, glycidic acid, by the action of alcoholic potassium hydroxide upon a mixture of the two isomeric chlorolactic acids. A whole series of homologous glycidic acids was obtained by P. G. Melikov and other investigators, by the use of this method.

In 1904 Darzens [2,3], and a year later Claisen [4], worked out a more convenient method for preparing these compounds. They resulted from the action of α-halogen esters upon aldehydes and ketones in the presence of dry sodium ethylate (Darzens) and sodium amide (Claisen).

These methods of preparation made the glycidic acids readily available compounds.

The first steps in the study of the chemistry of this new class of compounds had already been taken in 1881 by P. G. Melikov [5,6,7]. He showed that, when ordinary glycidic acid was heated with aqueous ammonia to 120° in a sealed tube, the oxide ring was opened and aminohydroxypropionic acid formed. Similar reactions were made with a whole series of glycidic acids, but the structure of the reaction products was never ascertained. It was only much later that E. Fischer [8] determined the structure of the reaction product of ammonia and glycidic acid. The oxide ring is opened at the side furthest from the carboxyl group, with the product of the reaction being isoserine, $H_2NCH_2CHOHCOOH$. The structure was determined by reducing the reaction product with hydriodic acid, as a result of which β-aminopropionic acid was obtained.

Erlenmeyer [9] showed that β-phenylglycidic acid adds ammonia at room temperature to form β-phenylisoserine.

$$C_6H_5-CH-CH-COOH + NH_3 \longrightarrow C_6H_5-CH(NH_2)-CH(OH)-COOH.$$
$$\qquad\qquad O$$

The structure was determined by comparing the reaction product with one obtained by another synthesis. Phenylisoserine was prepared by the reduction of nitrosophenylpyruvic acid.

$$C_6H_5C(=NOH)COCOOH.$$

A similar reaction was repeated by Forster and Rao [10] in 1926 and again by Fourneau and Billeter [11] in 1940. In the latter instance ethyl β-phenylglycidate was used as the starting material. When it was reacted with aqueous ammonia at a temperature of 0-4°, the ester was changed to the amide in less than a half hour. If the reaction mixture was then allowed to stand at room temperature for several days, the oxide ring was opened with the formation of the amide of β-phenylisoserine.

From the above review of the reactions of the glycidic acids with ammonia, it is apparent that the oxide ring is extremely unstable. It is also evident that the reaction product from ammonia and glycidic acid could have been obtained without resorting to higher temperatures as Melikov did.

However, the reactivity of the oxide ring changes markedly if the β-carbon atom becomes tertiary. For example, it was shown by Claisen [12] that ethyl β,β'-phenylmethylglycidate did not have its oxide ring opened at room temperature by ammonia and only formed the amide with difficulty. Fourneau and Billeter, loc. cit., also pointed out the great stability of the oxide ring in similar glycidic acids. They also concluded that the now-accepted formulas for these compounds do not reflect their properties. Because of this some authors avoided working with glycidic acids containing a tertiary carbon atom in the β-position.

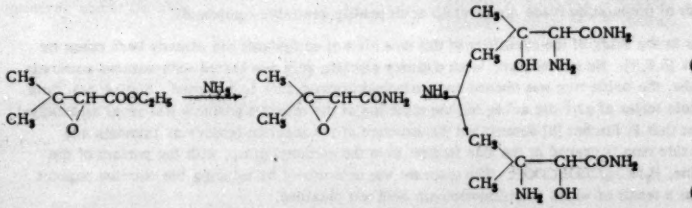
It was decided to fill this gap in the chemistry of glycidic acids by studying the action of ammonia upon glycidic acids with a tertiary carbon atom in the β-position. For the first example we took β,β'-dimethylglycidic acid ethyl ester. It is true, that Abderhalden [13] in 1934 studied the reaction of ammonia with β,β'-dimethyl-

glycidic acid, but when he obtained an uncrystallizable mixture, he did not investigate it any further.

First the reaction between ammonia and the ester of this acid at low temperatures was studied. The reaction was run in a closed tube with 30% aqueous ammonia for 4-5 hours at a temperature of 50°. In this way the amide of β,β'-dimethylglycidic acid was isolated in the form of white needlelike crystals. Finally the amide was obtained by shaking aqueous ammonia with the glycidic ester at room temperature for several hours. If the ammonia reacts with the glycidic ester at 100°, along with the formation of the amide, a splitting of the oxide ring occurs. After removal of the ammonia and the water, there results, not a crystalline substance as in the case of the amide, but a tar-like, uncrystallizable mass (as was reported by Abderhalden). In order to separate the product, the reaction mixture was dissolved in absolute ethanol and a stream of dry hydrogen chloride was passed into the solution. This resulted in separation of a crystalline precipitate which, as it was shown, turned out to be the hydrochloride of the amide of hydroxyaminoisovaleric acid (yield 5% of theory).

It is thus apparent that the oxide ring of this glycidic acid is opened at the relatively low temperature of 100°. Finally this reaction was effected in the absence of heat. The ammonia and the glycidic ester were allowed to stand at room temperature for a period of one month. The same product was obtained as when they were heated. Thus, the idea of the extreme stability of the oxide ring of glycidic acids containing a tertiary carbon atom in the β-position appears to be somewhat exaggerated.

In this case the opening of the oxide ring of the glycidic acid could occur in two separate directions.



(1)

(2)

The structure of the product had to be determined. This was done both directly and indirectly. The indirect method was to compare the product with one already reported in the literature. For this purpose α-amino-β-hydroxyisovaleric acid $(CH_3)_2C(OH)CH(NH_2)COOH$, which was prepared by Abderhalden [14] from β,β'-dimethylacrylic acid by means of a well-known literature method, was used. He also prepared the N-monobenzoyl derivative of this acid.

The free acid was prepared from the amide by hydrolysis with 50% sulfuric acid. The acid obtained melted at 259-260° in a closed capillary, while the acid obtained by Abderhalden melted at 218°. The monobenzoyl derivative of hydroxyaminoisovaleric acid was also obtained by reacting a solution of the amide in sodium hydroxide solution with benzoyl chloride, followed by the splitting of the amide linkage with nitrous acid. The benzoyl derivative obtained melted at 168-170°, while that of Abderhalden melted at 153°.

Therefore, it can be concluded that the product obtained is apparently the amide of α-hydroxy-β-aminoisovaleric acid.

Direct determination of the structure of the obtained product was made by reducing the hydroxyl to a hydrogen by means of hydriodic acid. Either α-amino- or β-aminoisovaleric acid should have been obtained. These are both well known and are readily distinguished by means of their melting points. α-Aminoisovaleric acid melts at 298°, the β-form at 217°. The product obtained melted sharply at 216-217°, and gave the correct analysis for aminoisovaleric acid.

Thus the second, direct, determination gives the same result as the first, indirect, method. This shows beyond doubt that the oxide ring of β,β'-dimethylglycidic acid is opened at the tertiary carbon atom by the action of ammonia, with the formation of the amide of α-hydroxy-β-aminoisovaleric acid.

EXPERIMENTAL

(With N. A. Rozepin and Z. M. Gofung)

Preparation of ethyl β,β'-dimethylglycidate. The method of Darzens, the reaction of acetone with ethyl

chloroacetate in the presence of alcohol free sodium ethylate was used. The yield in the best cases was 50%, based upon the ethyl chloroacetate which reacted.

After two redistillations the product boiled at 99-100° at 50 mm.

d_4^{20} 1.0110; n_D^{20} 1.4203; MR_D 36.70; calc. 36.75.

Reaction of β,β'-dimethylglycidate with ammonia in an aqueous medium. 10 g of ethyl β,β'-dimethylglycidate and 50 ml of 30% aqueous ammonia (d 0.885) were heated to 100° for 8 hours in a closed tube. The tube was then opened and its contents evaporated on a water bath in an evaporating dish. A clear brown tar resulted, which did not crystallize even on prolonged standing. The tarry product was dried in a vacuum desiccator and dissolved in absolute methanol. A stream of dry hydrogen chloride was passed into this solution over a 3 hour period. The reaction mixture warmed up and had to be cooled with ice water. The white precipitate of the hydrochloride of α-hydroxy-β-aminoisovaleric amide was filtered off and recrystallized from absolute alcohol. 5 g of well-formed, cubic crystals was obtained, which corresponds to 51% of theory.

0.4657 g substance: 54.4 ml 0.1 N H_2SO_4. 0.5163 g substance: 61.7 ml 0.1 N H_2SO_4. 0.1275 g substance: 0.1117 g AgCl. 0.1219 g substance: 0.1066 g AgCl. Found %: N 19.8, 20.3; Cl 21.17, 21.31. $C_5H_{13}O_2N_2Cl$. Calculated %: N 20.2; Cl 21.8.

Preparation of the benzoyl derivative. 0.5 g of the hydrochloride of α-hydroxy-β-aminoisovaleric amide was dissolved in a small amount of 10% NaOH. Benzoyl chloride, 1.2 g (1.5 times more than the theoretical) was added in small portions to the solution. The amount of benzoyl chloride was calculated for the dibenzoyl derivative. The reaction mixture was shaken violently. An insignificant amount of heat was given off. The unreacted benzoyl chloride was destroyed by warming the reaction mixture on the water bath. The reaction mixture was alkaline (tested with litmus).

The precipitate of the benzoyl derivative of α-hydroxy-β-aminoisovaleric amide (analysis showed that it was the monobenzoyl derivative) was filtered off on a Schott filter, carefully washed with water until completely alkaline-free, and recrystallized from absolute ethanol. 0.4 g of the monobenzoyl derivative of α-hydroxy-β-aminoisovaleric amide was obtained, which corresponds to 57 % of theory. M.p. 155-156°.

0.08 g substance: 8.45 ml N_2 (21°, 753 mm). 0.0836 g substance: 8.7 ml N_2 (23°, 772 mm). Found %: N 11.96, 11.97. $C_{12}H_{16}N_2O_2$. Calculated %: N 11.86.

Preparation of α-hydroxy-β-aminoisovaleric acid. 2 g of the hydrochloride of α-hydroxy-β-aminoisovaleric amide and 50 ml of 50% sulfuric acid (d 1.4) were heated for 7-8 hours in a round-bottomed flask with a reflux condenser. The SO_4^{2-} was removed with $BaCO_3$ until a negative reaction was obtained. The filtrate was evaporated on the water bath in an evaporating dish. A residue of a light-green, noncrystallizing, tarlike mass was obtained, which was dissolved in the minimum quantity of absolute ethanol after being dried in a vacuum desiccator. On cooling a white, halogen-containing (Beilstein test), finely-crystalline precipitate formed.

The halogen was removed with a silver sulfate solution. The AgCl precipitate was filtered off and the SO_4^{2-} was removed with $BaCO_3$ until a negative reaction for SO_4^{2-} was obtained. The filtrate was evaporated on the water bath in an evaporating dish. A tarry residue was obtained, which was dried in a vacuum desiccator and dissolved in absolute ethanol by prolonged heating. A finely crystalline, white precipitate separated on cobling. It was recrystallized from absolute ethanol. The product obtained did not contain halogen (Beilstein test).

0.3 g of α-hydroxy-β-aminoisovaleric acid was obtained, which corresponds to 20% of the theoretical yield. The melting point in a closed capillary was 259-260° (the substance darkens and gives off a considerable amount of gas).

0.0488 g substance: 4.6 ml N_2 (22°, 765 mm). 0.0670 g substance: 6.2 ml N_2 (22°, 762 mm). Found %: N 10.79, 10.56. $C_5H_{11}O_3N$. Calculated %: N 10.52.

Preparation of the monobenzoyl derivative of α-hydroxy-β-aminoisovaleric acid. An alcoholic solution of 0.5 g of the monobenzoyl derivative of α-hydroxy-β-aminoisovaleric amide was acidified with the minimum quantity of concentrated hydrochloric acid (acid to Congo) and treated with 0.2 g of $NaNO_2$ (the calculated quantity of $NaNO_2$ was used). The reaction mixture was shaken well and cooled with ice water. The reaction mixture

slowly became turbid, and then the crystalline precipitate of the monobenzoyl derivative of α-hydroxy-β-aminoisovaleric acid separated. The precipitate was recrystallized from a mixture of benzene and petroleum ether. It was extremely difficult to dissolve, and a prolonged period of heating on the steam bath was found necessary. 0.3 g of the substance was obtained, which corresponds to 60 % of the theoretical yield. M.p. 168-170°.

0.0566 g substance: 3.05 ml N_2 (22°, 762 mm). 0.1531 g substance: 8.3 ml N_2 (23°, 760 mm). Found %: N 6.14, 6.13. $C_{12}H_{15}O_4N$. Calculated %: N 5.90.

Reduction of α-hydroxy-β-aminoisovaleric acid. 0.4 g of the substance, 8 ml of hydriodic acid (d 1.9) and 0.2 g of red phosphorus, were heated to 140-150° in a sealed tube for 5 hours. The tube was then opened (no inside pressure was observed). The colorless contents (the red phosphorus was all gone) of the tube were diluted with 100 ml of water and taken almost to dryness in vacuo. The residue was once more diluted with water and the halogen was removed with silver sulfate while the SO_4^{2-} was separated with $BaCO_3$ until a negative test was given. A pasty, tarlike mass remained in the dish. It was very soluble in water and insoluble in absolute alcohol and ether. It was dissolved by heating in aqueous ethanol and, after, standing for a week, a finely crystalline precipitate separated. It was recrystallized from aqueous ethanol. M.p. 205° in a closed capillary. After being dried for 3 hours at 110° its melting point was 216°. 0.7 g was obtained, which corresponds to 20% of theory. The preparation was repeated.

0.0587 g substance: 6.2 ml N_2 (20°, 748 mm). 0.0650 g substance: 6.7 ml N_2 (20°, 772 mm). Found %: N 11.93, 12.01. $C_5H_{11}O_3N$. Calculated %: N 11.65.

SUMMARY

1. The reactions of ethyl β,β'-dimethylglycidate with aqueous ammonia have been studied. It was shown that when the glycidic ester was heated with 30% aqueous ammonia to 100°, the ester group was changed to the amide, and, at the same time, the oxide ring was opened. As a result, the amide of α-hydroxy-β-aminoisovaleric acid was formed.

2. The monobenzoyl derivative of the amide of α-hydroxy-β-aminoisovaleric acid, α-hydroxy-β-aminoisovaleric acid, and its monobenzoyl derivative were synthesized.

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STUDY OF COMPOUNDS CONTAINING A THREE-MEMBERED OXIDE RING

II. THE REACTION OF ETHYL β,β'-DIMETHYLGLYCIDATE WITH HYDROGEN SULFIDE

V. F. Martynov and N. A. Rozepina

Only a limited amount of studies have been devoted to the question of the reaction of hydrogen sulfide with compounds containing a three-membered oxide ring. The majority of these used ethylene oxide as the organic component. The papers of Chichibabin and Bestuzhev [1] and Nenitezescu and Scarlatescu [2] are included in this group, while Smith and Syöberg [3] used a more complex substance, glycide. As for the reaction of glycidic acids with hydrogen sulfide, there is nothing in the literature, even though these compounds may be of considerable interest.

A study of the reaction of hydrogen sulfide with glycidic acid containing a tertiary carbon atom in the β-position was undertaken. Ethyl β,β'-dimethylglycidate was chosen as the first representative, as it was the most readily available. Several methods were used to study the reaction of hydrogen sulfide with the above glycidic ester. A mixture of the glycidic ester and a saturated solution (in the cold) of hydrogen sulfide in aqueous ethanol was heated in a closed tube in the presence or the absence of mineral acids. In all of these cases no addition of hydrogen sulfide occurred, but the oxide ring hydrolyzed to form ethyl β,β'-dimethylglycerate. This reaction occurred even when the alcohol contained only traces of water. Only when absolute alcohol was used was the hydrolysis absent, but even then no addition of hydrogen sulfide occurred. The failure of these experiments is apparently due to the fact that glass tubes were used, and a large amount of hydrogen sulfide could not be placed in the reaction zone. The method of Smith and Syöberg [3] was then used. They found that the addition of hydrogen sulfide to the glycide occurred at room temperature in the presence of a large amount of $Ba(OH)_2$. Barium hydroxide acts as catalyst in this case, as there are many examples of the increase of the lability of the oxide ring under basic conditions.

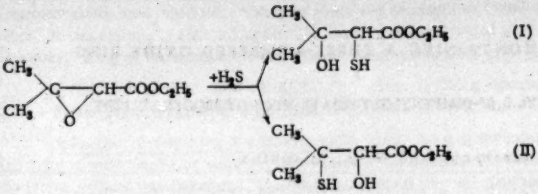
The following method was used: $Ba(OH)_2$, more than one mole per mole of glycidic ester, was mixed with a small amount of water and, while the solution was being stirred continuously, a stream of hydrogen sulfide was passed through it. After some time (2-3 hours) an alcoholic solution of the glycidic ester was added dropwise, while the stirring and the passage of hydrogen sulfide was continued. After completion of the addition of the glycidic ester, the hydrogen sulfide was passed in for 2-3 hours more. The barium was then completely precipitated with carbon dioxide, and the filtrate distilled until layers separated in the distillation flask. The lower layer appeared to be the reaction product and was extracted with ether.

A fractional distillation of the reaction products of several experiments revealed that the main part of the ethyl β,β'-dimethylglycidate had reacted with hydrogen sulfide. In each case only an insignificant quantity of the starting glycidic ester was recovered.

The sulfur-containing substance amounted to 70-75% of the theoretical. However, it was not a homogeneous substance, since on fractional distillation a series of fractions were obtained. The first of these, constituting almost half of the total amount, boiled over the narrow range of 97-99°, at 8 mm. The rest of the substance did not have a narrow-range boiling point, but distilled in the interval 130-175°.

The fraction with the boiling range of 97-99° had an unpleasant, penetrating odor. It gave a positive test for sulfur and for the mercaptan group (Reinboldt's test, mercuric mercaptide), and in all of the determinations (percent of total sulfur, mercury in the mercaptide, molecular weight, and molecular refractivity) it corresponded to ethyl hydroxymercaptoisovalerate.

In order finally to establish the structure of the compound, the position of the hydroxyl and mercapto group in the molecule had to be determined, as there are two possible ways in which the oxide ring could be opened:



The choice between the two formulas could have been made by determining the position of either the mercapto or of the hydroxyl group. It is well known from the literature that primary and secondary mercaptans give a red color with nitrous acid, while tertiary mercaptans give a green color. This is the qualitative test of Reinboldt [4]. No exception to this test has been found even though it has been tested with many types of compounds. The compound obtained gave a red coloration with this reaction and, on this basis, could be assigned the structure of Formula (I), ethyl α-mercapto-β-hydroxyisovalerate. In order to prove the correctness of Reinboldt's test, the position of the hydroxyl group in the molecule had to be determined.

To attain this, the mercaptan group had to be removed from the molecule, giving one of two possible acids: either β-hydroxyisovaleric or α-hydroxyisovaleric acid. Both of these acids are well known and can be distinguished from each other by the following property: β-hydroxyisovaleric acid is a syrup, while α-hydroxyisovaleric acid is a crystalline solid, melting at 86°. The mercaptan group was removed by the method of Mozingo [5] by heating the substance in alcohol with a large quantity of Raney nickel. As a result, an ethyl hydroxyisovalerate was obtained, which on saponification, gave an acid which did not crystallize even after a long period of standing (almost a month). Thus after the removal of the mercaptan group, β-hydroxyisovaleric acid was obtained.

The second method of determination agreed with the first. The oxide ring of ethyl β,β'-dimethylglycidate is opened by hydrogen sulfide in basic media at the site of the carboxyl group, and α-mercapto-β-hydroxyisovalerate is formed.

The nature of the higher boiling fraction could not be determined in spite of many attempts. It can be pointed but, however, that although these fractions contained sulfur, they did not give a test for the mercaptan group.

EXPERIMENTAL

Reaction of ethyl β,β'-dimethylglycidate with hydrogen sulfide in the presence of $Ba(OH)_2$. 20 g of $Ba(OH)_2$ was mixed with 100 ml of water, and a stream of hydrogen sulfide was passed into the mixture for 2 hours with continuous stirring. Then, while the stirring and the passage of hydrogen sulfide was continued, a solution of 40 g of the glycidic ester in 80 ml of ethanol was dropped in from a dropping funnel. The hydrogen sulfide was passed in for 3 hours more after all of the substance had been added.

The reaction mixture was allowed to stand overnight. The next day, a stream of carbon dioxide was passed in for 5 hours, with continuous stirring. The $BaCO_3$ was filtered off, the ethanol was distilled, and the reaction product separated at the bottom as an oily liquid. It was extracted with ether. The ethereal extract was dried with $MgSO_4$. After distillation of the ether, a vile-smelling liquid remained. This was vacuum distilled at 10 mm. Three fractions were obtained: 1) 97-99°, 10 g; 2) 140-150°, 7 g; 3) 165-170°, 3.7 g; 4) intermediate fractions, 1.5 g; and 5) residue in the distillation flask, 1.2 g. Total 23.4 g, corresponding to 47% of the theoretical. The first fraction analyzed as follows: d_4^{23} 1.097; n_D^{23} 1.46262; MR_d 44.56; calculated 44.03.

0.1173 g substance: 0.2325 $BaSO_4$. 0.2557 g substance: 0.3344 g $BaSO_4$. 0.1853 g substance: 17.61 g benzene: Δt 0.319°, 0.1411 g substance; 16.52 g benzene: Δt 0.255°. Found %: S 18.06, 17.96; M 171, 173.5. $C_7H_{14}O_3S$. Calculated %: S 18.02; M 178.

Mercuric mercaptide was obtained from the first fraction. The substance was shaken with three volumes of absolute ethanol and three times its weight of red mercuric oxide was added to it. The reaction proceeded

with the evolution of heat. A white precipitate of the mercaptide separated, which, after recrystallization from absolute ethanol, was analyzed for mercury.

0.1071 g substance: 3.9 ml NH_4CNS. 0.1118 g substance: 4.1 ml NH_4CNS. Found %: H 36.4, 36.65. $C_{14}H_{26}O_6S_2Hg$. Calculated %: Hg 36.21.

Removal of the sulfur from ethyl α-mercapto-β-hydroxyisovalerate. The sulfur was removed by the hydrolysis of the substance with Raney nickel according to Mozingo [5]. A catalyst of the highest activity was used.

6 g of the substance mixed with 60 ml of a suspension of Raney nickel in absolute ethanol (approximately 30-35 g of the catalyst). The mixture was refluxed for 8 hours, the catalyst was filtered off, and, after the removal of the alcohol, a fragrant liquid was obtained. It distilled over a one degree range at 62° and 7 mm. 3.5 g corresponding to 71.5% of theoretical was obtained. A negative test for a mercaptan group was obtained.

d_4^{20} 0.975; n_D^{20} 1.4187; MR_D 37.79, calculated 37.705.

The obtained ester was saponified by warming it with an alcoholic solution of sodium hydroxide. The resultant salt was acidified with dilute sulfuric acid and the free acid extracted with ether in an extractor. The ether extract was dried with magnesium sulfate and, after removal of the ether, a syrupy liquid with a sharp odor was obtained. It did not crystallize even upon standing for a month in a desiccator. The acid was analyzed as its silver salt:

0.1251 g substance: 0.0602 g Ag. 0.1543 g substance: 0.0744 g Ag. Found %: Ag 48.23, 48.35. $C_5H_9O_3Ag$. Calculated %: Ag 48.06.

SUMMARY

1. The reaction between hydrogen sulfide and ethyl β,β'-dimethylglycidate in the presence of $Ba(OH)_2$ at room temperature has been studied. It has been shown that under these conditions an addition of hydrogen sulfide occurs, with the formation of ethyl α-mercapto-β-hydroxy isovalerate.

2. It was shown that Reinboldt's test was valid for compounds containing a carboxyl and a carbomethoxyl group in the α-position to the mercaptan group.

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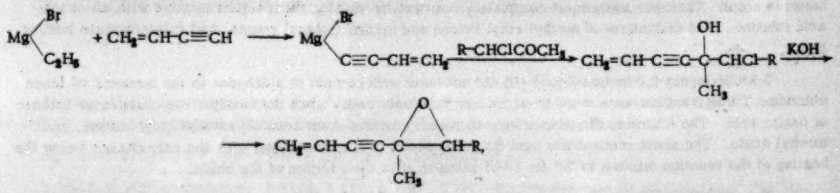
THE REACTION OF VINYLACETYLENIC α-OXIDES WITH OXYGEN-CONTAINING COMPOUNDS AND ORGANOMAGNESIUM COMPOUNDS

F. Ya. Perveev and N. I. Kudryashova

In spite of the large number of papers on the physical and chemical properties of oxides, no vinylacetylenic oxides have been reported up to the present time. It was considered expedient to find a method of synthesizing these compounds and to determine the influence of the vinylacetylene group on the reactivity of the oxide, and on the order of addition of various compounds. The synthesis of the oxides was accomplished by starting with vinyl acetylenic chlorohydrins, which were obtained by the reaction of the vinylacetylenyl magnesium halides with α-chloroketones and α-chloroaldehydes.

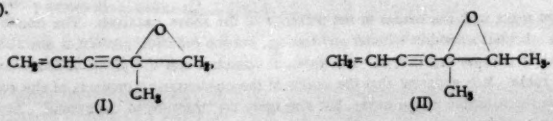
The condensation of vinylacetylene with chloroacetone and chloromethyl ethyl ketone (3-chlorobutanone-2) was studied. The synthesis of the oxide occurs according to the following equation:



where R= H and CH_3.

The HCl was removed by the action of powdered potassium hydroxide on an ethereal solution. The oxides were obtained in yields of 80-85% based on the chloroketone used.

The oxides synthesized were 2-methylepoxy-1,2-hexen-5-yn-3 (I) and 3-methylepoxy-2,3-hepten-6-yn-4 (II).

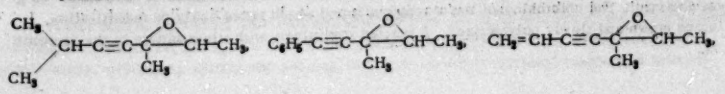


They are colorless liquids with a sharp odor. On exposure to the air they slowly thicken, and, after 2-3 months, form transparent, glasslike masses. They are thermally unstable, and, when heated above 140°, in the absence of a solvent, they explode.

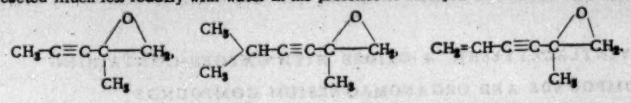
The oxides obtained are somewhat distinguishable by differences in reactivity. For example, 2-methylepoxy-1,2-hexen-5-yn-3 (I) decomposes explosively upon the addition of a crystal of ferric chloride, even at room temperatures. 3-Methylepoxy-2,3-hepten-6-yn-4 (II) remains unchanged in the presence of ferric chloride.

Oxide (I) is changed into the glycol by the action of water containing traces of hydrochloric acid, whereas oxide (II) is preferentially isomerized to the corresponding ketone under these conditions. The glycol is formed in the presence of traces of sulfuric acid. The addition of water to the oxides occurs readily. The reaction starts at room temperature and proceeds with the evolution of much heat.

The ease of the addition of water to ethylenic oxides, as was shown by Eltekov [2], depends on the number and the position of the substituents. It was shown [3] that the trisubstituted acetylenic and vinylacetylenic oxides



reacted much less readily with water in the presence of catalysts than did the disubstituted asymmetric oxides.



Several authors have proposed different mechanisms for the addition of water to the oxides. Zimakov [1] showed that ethylene glycol is formed by means of an intermediate compound (ethyl glycol sulfuric ester). However, this is a common characteristic. It is proposed that the catalytic activity of the various acids on the rupture of the oxide ring lies in the fact that the proton of the acid coordinates with the oxygen atom of the oxide ring, and the anion, by reaction with the water, generates hydroxyl groups which complete the splitting of the oxide ring by adding to the more polarized carbon atom. 2-Methyl-epoxy-1,2-hexen-5-yn-3 (I) easily adds aldehydes and ketones in the presence of ferric chloride, forming the corresponding acetals – dioxolanes.

The reaction of the oxides with acetone, methyl ethyl ketone, methyl isobutyl ketone, and mesityl oxide was studied.

The method used for the condensation of the ketones with the oxide is as follows: 1-2 g of the catalyst was added to three times the quantity of the ketone. The oxide was then added to it in small portions. The addition of the oxide was regulated so as to keep the reaction temperature below 40°. The mixture turned dark brown in color. The color was almost completely removed by washing the reaction mixture with an oxalic acid solution. The derivatives of methyl ethyl ketone and methyl isobutyl ketone had indeterminate boiling points.

3-Methylepoxy-2,3-hepten-6-yn-4 (II) did not react with ketones or aldehydes in the presence of ferric chloride. These reactions were found to occur comparatively easily when the catalyst was changed to sulfuric or oxalic acid. The following dioxalanes were obtained: derived from acetone, methyl ethyl ketone, and mesityl oxide. The above method was used for the synthesis of the dioxolanes, with the only change being the heating of the reaction mixture to 70° for 10-15 minutes after the addition of the oxide.

The dioxolanes were hydrolyzed to the corresponding glycol and ketone by warming them in 2% sulfuric acid. This served as a method for the determination of the structure of the products of the condensation between the oxides and the ketones. The ketones were identified by means of their 2,4-dinitrophenylhydrazones.

The cyclic acetals are colorless liquids with slight pleasant odors. They slowly turn yellow on exposure to air. They are thermally unstable, and explode when heated above 140°.

Acetoacetic ester does not react with the oxides in the presence of the above catalysts. The condensation reaction with chloroacetone proceeds smoothly without any tarring, but the reaction product is unstable and decomposes when it is heated in vacuum at 1-2 mm. The physical constants and the yields of the dioxolanes synthesized is given in the table. It is apparent that the yields of the condensation products of the oxides and ketones depend not only upon the structure of the oxide, but also upon the structure of the ketone. Asymmetric disubstituted vinylacetylenic oxides react more readily with ketones than do trisubstituted ones. The yield does not depend upon the chain length of the substituent, but upon its branching. For example, the derivatives of acetone and methyl ethyl ketone are obtained in yields of 52-67% whereas the yield of the derivative of methylisobutyl ketone never exceeds 25%. The isomerization products of the oxides, and small amounts of tars due to polymerization, were obtained as side reaction products in all of these condensations. The side products were not investigated further.

EXPERIMENTAL

2-Methyl-1-chlorohexen-5-yn-3-ol-2. 80 g of dry vinylacetylene was passed into a solution of ethyl magnesium bromide (1 mole) in ether with strong stirring and cooling with ice and water. The reaction mixture was allowed to stand overnight. 85 g of chloroacetone was then added slowly to it and the stirring continued for 3 hours more. The organomagnesium complex obtained was then carefully decomposed, with cooling, by 30% acetic acid. The ether layer was separated, washed with water, and dried with fused Na_2SO_4. After the removal of the ether, the residue was vacuum distilled. The chloroalcohol obtained had a b.p. of 70-71° at 5 mm. 76 g of the substance was obtained. The chloroalcohol was a colorless liquid which tarred badly on redistillation. Upon exposure it turned brown and slowly polymerized. It reacted explosively with silver nitrate in the presence of strong nitric acid.

No.	Formula	B.p.	d_4^{17}	n_D^{17}	MR_D	
					calculated	found
1	$CH_2=CH-C\equiv C-C(CH_3)-CH_2-O-C(CH_3)_2-O$	51-52°/3 mm	0.9448	1.4658	47.0	48.5
2	$CH_2=CH-C\equiv C-C(CH_3)-CH_2-O-C(CH_3)(C_2H_5)-O$	71-72°/4 mm	0.9440	1.4680	51.5	53.0
3	$CH_2=CH-C\equiv C-C(CH_3)-CH_2-O-C(CH_3)(C_4H_9)-O$	92-93°/5 mm	0.9378	1.4675	60.6	61.7
4	$CH_2=CH-C\equiv C-C(CH_3)-CH(CH_3)-O-C(CH_3)_2-O$	60-61°/5 mm	0.9225	1.4690	52.7	54.3
5	$CH_2=CH-C\equiv C-C(CH_3)-CH(CH_3)-O-C(CH_3)(C_2H_5)-O$	80-81°/5 mm	0.9390	1.4750	55.8	57.7
6	$CH_2=CH-C\equiv C-C(CH_3)-CH(CH_3)-O-C(CH_3)(C_4H_9)-O$	99-103°/10 mm	0.9391	1.4730	65.5	66.4
7	$CH_2=CH-C\equiv C-C(CH_3)-CH(CH_3)-O-C(CH_3)(C_4H_7)-O$	89-92°/3 mm	0.9515	1.4850	65.0	66.4

In view of this decomposition of the chloroalcohol upon redistillation, it was not isolated in the subsequent runs and the oxide was obtained directly from the dry ether solution of the chloroalcohol.

d_4^{20} 1.0816; d_4^0 1.1034; n_α^{20} 1.49976; MR_α 39.0; calculated 38.3.

0.1508, 0.1703 g substance: 0.1504, 0.1698 g AgCl; 0.0861 g substance: 14.22 ml CH_4 (11.9° 760 mm); 0.1339 g substance: 23.82 ml CH_4 (16.5°, 749 mm). Found %: Cl 24.7, 24.61; active H 0.703, 0.732. C_7H_9OCl. Calculated %: Cl 24.55; active H 0.700.

3-Methyl-2-chlorohepten-6-yn-4-ol-3 was obtained in a manner similar to the above. After two redistillations a product with a b.p. of 69° at 3.5 mm was obtained.

d_4^{20} 1.0606; d_4^0 1.1482; n_α^{20} 1.49416; MR_α 43.3; calculated 42.9

0.1839, 0.2405 g substance: 0.1631, 0.2147 g AgCl. Found %: Cl 21.9, 22.08. $C_8H_{11}OCl$. Calculated %: Cl 22.4.

2-Methylepoxy-1,2-hexen-5-yn-3 (I). 110 g of powdered potassium hydroxide was added in small portions with continuous shaking to a solution of 90 g of the chloroalcohol in 300 ml of absolute ether. The ether solution was then carefully poured off and the residue dissolved in water. The aqueous layer was twice extracted with ether. The ether extracts were added to the ether solution and dried over Na_2SO_4. The ether was distilled off. The residual oxide after two redistillations had a boiling point of 50-51° at 15 mm. Yield 72%.

d_4^{22} 0.9149; d_4^0 0.9377; n_α^{22} 1.47394; MR_α 33.17; calculated 31.3.

0.1048 g substance: 0.2910 g CO_2; 0.0870 g H_2O. Found %: C 77.48; H 9.51. C_7H_8O. Calculated %: C 77.75; H 9.39.

3-Methylepoxy-2,3-hepten-6-yn-4 (II). The oxide was obtained in the first run by using the above method. It boiled at 54-55° at 12 mm after two redistillations.

d_4^{20} 0.9005; n_D^{20} 1.4781; MR_D 38.41; calculated 36.82.

0.1034, 0.1537 g substance: 0.2973, 0.3084 g CO_2; 0.0778, 0.0875 g H_2O. Found %: C 78.14, 78.09; H 8.45, 8.45. $C_8H_{10}O$. Calculated %: C 78.63; H 8.25.

Later both of the oxides were obtained directly from the ether solution of the chloroalcohol without first isolating and redistilling it. $^3/_4$ of a mole of the chloroketone (chloroacetone or chloromethyl ethyl ketone) was added slowly, with strong stirring and cooling, to 1 mole of vinylacetylenyl magnesium bromide. After addition

of the chloroketone, the stirring was continued for 3-4 hours. The organomagnesium complex was decomposed with stirring and cooling by 30% acetic acid.

The ether layer was separated, and the water twice extracted with ether. The ether extracts were combined with the ether solution, washed with water, and dried. The ether solution was filtered and the oxide was obtained by the method given above. In this case the yield of the oxide was 85-87% of theory, based on the chloroketone used.

2-Methylhexen-5-yn-3-diol-1,2. 90 ml of water and 3 drops of hydrochloric acid were placed in a flask. 30 g of the oxide (I) was added in small portions with continuous shaking. An evolution of heat occurred. In order to avoid too much tarring, the flask was cooled from time to time in ice water. At the end of the reaction, the water was vacuum distilled, and the resultant dark-brown mass was placed into a crystallizing dish immersed in a freezing mixture (ice and salt). The crystals which separated were filtered off and recrystallized from benzene. After three recrystallizations, colorless crystals (17 g, 50% of the theoretical) with a m.p. of 48-49° and a b.p. of 81-82° at 3 mm were obtained.

0.1088 g substance: 40.62 ml CH_4 (12.5° 753 mm); 0.1097 g substance: 41.22 ml CH_4 (15.3° 766 mm); 0.1052, 0.1067 g substance: 0.2585, 0.2627 g CO_2; 0.0770, 0.0794 g H_2O. Found %: C 67.01, 67.15; H 8.19, 8.33; active H 1.573, 1.559. $C_7H_{14}O_2$. Calculated %: C 66.64; H 7.99; active H 1.587.

3-Methylhepten-6-yn-4-diol-2,3. The glycol was obtained under conditions similar to the above after working it up with water containing 5 drops of sulfuric acid. The reaction was accompanied by an evolution of heat but with less intensity then in the preceding case. The upper layer which formed, was removed and the aqueous layer was extracted with ether. The ether solution was added to the main fraction and dried with Na_2SO_4. The ether was removed and the substance obtained was vacuum distilled. After two redistillations, the glycol had a b.p. of 109-110° at 8 mm.

d_4^1 1.0166; d_4^{16} 1.008; n_D^{16} 1.5010; MR_D 41.2; calculated 39.6.

0.1066, 0.1012 g substance: 36.2, 34.2 ml CH_4 (14.5°, 756 mm). Found %: active H 1.423, 1.416. $C_9H_{12}O_2$. Calculated %: active H 1.438.

The glycol obtained was a viscous liquid which slowly crystallized. M.p. 20-21°. The crystals polymerized to a hard glasslike mass on exposure to the air.

Condensation of 2-methylepoxy-1,2-hexen-5-yn-3 (I) with acetone. 100 ml of acetone was placed with 1 g of ferric chloride in a round-bottomed flask with a reflux condenser and a mechanical stirrer. 20 g of the oxide was added slowly so as not to allow the temperature to rise above 40°. After all of the oxide was added, the stirring was continued for about one hour. The mixture was then washed with a solution of oxalic acid, and dried with Na_2SO_4. The acetone was removed in vacuum. After two redistillations, 16 g (52%) of the substance was obtained. Its constants are given in the table (Formula 1).

0.1063, 0.1105 g substance: 0.2806, 0.2922 g CO_2; 0.0822, 0.0846 g H_2O. Found %: C 71.99, 72.12; H 8.65, 8.57. $C_{10}H_{14}O_2$. Calculated %: C 72.26; H 8.49.

Hydrolysis of the dioxolane. 10 g of the dioxolane and 100 ml of a 2% solution of H_2SO_4 were placed in a round bottom flask with a mechanical stirrer and reflux condenser. The mixture was heated for 30 minutes. Acetone was separated from the products of the hydrolysis and identified by means of its 2,4-dinitrophenylhydrozone, which melted at 125°. A mixed melting point determination with an authentically prepared acetone 2,4-dinitrophenylhydrazone gave no depression.

Found %: N 23.7. $C_9H_{10}O_4N_4$. Calculated %: N 23.51.

The aqueous solution, after removal of the acetone, was distilled. The distillate was extracted with ether, the ether extracts were dried with Na_2SO_4, the ether was removed, and the residue vacuum distilled. Along with the glycol, a crystalline substance with a melting point of 91-92° and a b.p. of 81-82° at 3 mm was isolated. It gave a red coloration characteristic for enols with alcoholic ferric chloride, and could be titrated with dilute alkalis and sodium methylate.

Condensation of 2-methylepoxy-1,2-hexen-5-yn-3 (I) with methyl ethyl ketone. By the condensation of 30 g of the oxide with 50 ml of methyl ethyl ketone, 29 g (57%) of the dioxolane was obtained (Formula 2 in the table).

0.0997, 0.1102 g substance: 0.2674, 0.2952 g CO_2; 0.0781, 0.0857 g H_2O. Found %: C 73.15, 73.07; H 8.77, 8.70, $C_{11}H_{16}O_2$. Calculated %: C 73.30; H 8.95.

Methyl ethyl ketone was isolated from the hydrolysis products of the dioxolane and identified by means of its 2,4-dinitrophenylhydrazone with a m.p. of 110°, which gave no depression with an authentically prepared methyl ethyl ketone 2,4-dinitrophenylhydrazone.

Found %: N 22.40, 22.45. $C_{10}H_{12}O_4N_4$. Calculated %: N 22.20.

In addition, as in the first case, the dehydration product of the glycol was obtained.

Condensation of 2-methylepoxy-1,2-hexen-5-yn-3 (I) with methyl isobutyl ketone. The same method was used to condense 30 g of the oxide and 50 ml of methylisobutyl ketone. 14 g (25%) of the dioxolane (Formula 3 in the table) was obtained.

0.1034, 0.1058 g substance: 0.2820, 0.2887 g CO_2; 0.949, 0.965 g H_2O. Found %: C 74.39, 74.42; H 10.27, 10.21. $C_{12}H_{20}O_2$. Calculated %: C 74.60; H 10.11.

The hydrolysis products of the dioxolane were found to contain: 1) methyl isobutyl ketone, identified by means of its 2,4-dinitrophenyl hydrazone with a m.p. of 93-94°, which gave no depression in a mixed melting point determination.

Found %: N 19.99. $C_{13}H_{16}O_4N_4$. Calculated %: N 19.98

and 2) a crystalline product with a m.p. of 91-92°.

Condensation of 3-methylepoxy-2,3-hepten-6-yn-4 (II) with acetone. 100 ml of acetone and 4 g of oxalic acid were placed in a round bottomed flask with a mechanical stirrer and reflux condenser, and 20 g of the oxide was added slowly to it. The reaction temperature was kept around 40°. The mixture was then washed with aqueous sodium carbonate and dried with Na_2SO_4. The excess acetone was removed in vacuum and the residual dark brown product distilled at a temperature of 60-61° at 5 mm: 14 g (49%) of the substance was obtained. Its constants are given in the table (Formula 4).

0.1028, 0.1131 g substance: 0.2752, 0.3033 g CO_2; 0.0838, 0.0927 g H_2O. Found %: C 73.02, 73.13; H 9.12, 9.17. $C_{11}H_{16}O_2$. Calculated %: C 73.29; H 8.95.

The dioxolane was hydrolyzed with 2% H_2SO_4. The acetone 2,4-dinitrophenylhydrazone, m.p. 124°, which separated gave no depression in a mixed melting point determination. A ketone with a b.p. of 57-59° at 9 mm and an empirical formula of $C_9H_{16}O$, was isolated from the hydrolysis products.

d_4^{16} 0.9091; d_4^{0} 0.9207; n_D^{16} 1.4860; MR_D 38.5; calculated 36.7.

The semicarbazone of the ketone melted at 156-158° (with decomposition) after two recrystallizations from alcohol.

Found %: N 23.51, 23.47. $C_9H_{19}ON_3$. Calculated %: N 23.41.

In addition, a higher boiling fraction, b.p. 73-76° at 4 mm, which gave a red color characteristic for enols with an alcoholic solution of ferric chloride, was isolated from the hydrolysis products.

Condensation of 3-methylepoxy-2,3-hepten-6-yn-4 (II) with methyl ethyl ketone. The condensation was made using the above method. The reaction proceeded less energetically. After the addition of 25 g of the oxide, the reaction mixture was heated to 70° for 15 minutes. 13 g (33%) of the dioxolane, with a b.p. of 80-81° at 5 mm, was isolated (Formula 5 in the table).

0.978, 0.1018 g substance: 0.2651, 0.2763 g CO_2; 0.0798, 0.0845 g H_2O. Found %: C 73.93, 74.02; H 9.13, 9.23. $C_{12}H_{18}O_2$. Calculated %: C 74.19; H 9.34.

Methyl ethyl ketone was isolated from the hydrolysis of the dioxolane and characterized by means of its 2,4-dinitrophenylhydrazone, with a m.p. of 107-108°, which gave no depression in a mixed melting point determination.

Found %: N 22.45. $C_{10}H_{12}O_4N_4$. Calculated %: N 22.20.

The same products isolated from the acetone condensation were also obtained.

Condensation of 3-methylepoxy-2,3-hepten-6-yn-4 (II) with methylisobutyl ketone. The dioxolane was obtained by the condensation of 20 g of the oxide with a quantity (50 ml.) of methylisobutyl ketone under the same conditions. It had a b.p. of 99-103° at 10 mm. The yield was 3 g which corresponds to 8% of theory (formula 6 in the table).

0.1021, 0.1024 g substance: 0.2825, 0.2904 g CO_2; 0.0923, 0.0933 g H_2O. Found %: 75.46, 75.57; H 10.12, 10.20. $C_{14}H_{22}O_2$. Calculated %: C 75.63; H 9.95.

Methylisobutyl ketone was isolated on hydrolysis. Its 2,4-dinitrophenyl hydrazone melted at a temperature of 94-95°, and gave no depression in a mixed melting point determination.

Found %: N 20.01. $C_{13}H_{16}O_4N_4$. Calculated %: N 19.98

The dehydration products of the glycol were also isolated.

Condensation of 3-methylepoxy-2,3-hepten-6-yn-4 (II) with mesityl oxide. 8 g of the dioxolane (22%) with a m.p. of 89-92° was obtained from the condensation of 20 g of the oxide with mesityl oxide (Formula 7 in the table).

0.1043, 0.1054 g substance: 0.2911, 0.2939 g CO_2; 0.0874, 0.0869 g H_2O. Found %: C 76.12, 76.06; H 9.38, 9.21. $C_{14}H_{20}O_2$. Calculated %: C 76.32; H 9.15.

In addition, a fraction with a b.p. of 55-60° at 3 mm – a mixture of the ketone (isomerization product of the oxide) and the unreacted oxide – was obtained.

Upon hydrolysis of the dioxolane, the original mesityl oxide was isolated and characterized by means of its 2,4-dinitrophenylhydrazone with a m.p. of 199-200°, which gave no depression in a mixed melting point determination.

A considerable amount of a tarry product remained after the distillation of all of these dioxolanes. The distillation was made in the absence of air.

Condensation of methylepoxy-2,3-hepten-6-yn-4 (II) with methyl ethyl ketone in the presence of sulfuric acid. 50 ml of methyl ethyl ketone and 3-4 drops of sulfuric acid were placed in a round bottomed flask and 30 g of the oxide was slowly added to it. The reaction temperature rose to 60°. The mixture was then heated to 70° for 15 minutes, washed with aqueous sodium carbonate, and dried with Na_2SO_4. The excess of methyl ethyl ketone was removed in vacuum. The residue was distilled. 12 g of a substance with a b.p. of 58-62° at 4 mm, n_D^{18} 1.4940, (the product of the isomerization of the oxide – the ketone) and 23 g (49%) of the dioxolane with a b.p. of 78-80° at 4mm, n_D^{18} 1.4721, was obtained.

Methyl ethyl ketone and the product of the dehydration of the glycol were obtained from the products of the hydrolysis of the dioxolane. Thus, when 2-methylepoxy-2,3-hepten-6-yn-4 is reacted with methyl ethyl ketone in the presence of sulfuric acid, the yield of the dioxolane is greatly increased.

SUMMARY

1. Upon the reaction of vinylacetylenyl magnesium bromide with chloroacetone and chloromethyl ethyl ketone, the corresponding chloroalcohols, 2-methyl-1-chlorohexen-5-yn-3-ol-2 and 3-methyl-2-chloroheptene-6-yn-4-ol-3, were obtained.

2. The vinylacetylenyl oxides, 2-methylepoxy-1,2-hexen-5-yn-3 and 3-methylepoxy-2,3-hepten-6-yn-4, were obtained from these chloroalcohols by the action of powdered potassium hydroxide in ether solution.

3. The catalytic activity of ferric chloride, sulfuric acid, and oxalic acid upon the reaction of the oxides with ketones was studied. Some new dioxolanes, those of acetone, methyl ethyl ketone, methyl isobutyl ketone, and mesityl oxide, which are not reported in the literature, were obtained.

4. It was shown that the yields of the dioxalanes depends on the nature of the catalyst, the structural peculiarities of the oxides, and the structure of the ketone.

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NEW TYPES OF TERPENE TRANSFORMATIONS

IX. THE USE OF CHLOROTERPENES IN THE ORGANO-MAGNESIUM SYNTHESIS

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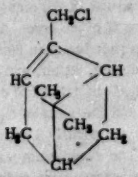
The chloroterpenes, initially obtained by the authors, are allylic chlorides suitable for a great variety of double decomposition reactions which may open up a new series of synthetic possibilities in the chemistry of terpenes. Some of these possibilities have already been realized [1]. The use of chloroterpenes in the organo-magnesium synthesis, in successful cases, would lead directly to a series of interesting syntheses of terpene derivatives of a definite structure, since rearrangements do not commonly occur during this reaction.

The task set is not a simple one. Allyl chloride, the prototype of the chloroterpenes, like other allyl halides, could not be reacted directly with magnesium for the preparation of homogeneous allyl magnesium chloride [2]. Later Yavorsky [3] avoided the difficulty of initially preparing the allyl magnesium halide and obtained allyl carbinols, although in low yields, by reacting a mixture of allyl bromide and a ketone with magnesium coated with ethyl bromide. He thus became the first to accomplish the synthesis originally proposed by Barbier [4]. Only in 1931 was Gilman [5] able to obtain an 80% yield of allyl magnesium chloride by using a large excess of magnesium, dilute ether solutions, and powerful stirring. Other researchers, repeating his work, could not obtain as high yields as he did [6].

Gilman was also the first to obtain allyl magnesium bromide in 89% yields, again by using very dilute ether solutions, a large excess of magnesium of a definite grade, and powerful stirring. Under other conditions, this yield could not even be approached [7]. Young, when studying the preparation of isobutenyl magnesium chloride, found that the yield dropped sharply when the reaction conditions were changed [8].

The above review shows that the use of allylic halides for reactions with magnesium is difficult, and this general problem has not been solved. The proper reaction conditions have to be found for each allylic halide. Any slight variation in these conditions will sharply affect the yield, or even make the reaction impossible. The magnesium has to be activated by coating with ethyl bromide, heating with iodine, etc. Allyl bromides will react more readily with magnesium than will allyl chlorides. For this reason the chloroterpenes will probably react less readily with magnesium than the corresponding bromoterpenes. Recognizing the great waste of time and reagents in survey experiments, the most readily available and stable of the chloroterpenes, myrtenyl chloride, was chosen for this study. Its preparation and properties were described earlier [9]. It is 10-chloro-α-pinene, $C_{10}H_{15}Cl$(A).



(A)

Throughout the rest of this paper the radical $C_{10}H_{15}$ represents the myrtenyl radical of the above structure.

In the reaction of magnesium with any halide, one or two reactions are possible:

(I) $R{-}Cl + Mg = R{-}Mg{-}Cl$; (II) $R{-}Mg{-}Cl + RCl = MgCl_2 + R{-}R$.

The yield from the first reaction may be determined by titrating an aliquot of the solution with acid; the yield of the second — by determination of the amount of inorganic chloride after the amount of the Grignard reagent has been found.

In order to find the conditions for myrtenyl chloride to react according to Reaction I, small amounts (2 g) of the chloride were used. Resublimed magnesium with a purity > 99.8% was used in the form of shavings of 30-60 mesh.

The first series of experiments was run according to Yavorsky's conditions. A solution of myrtenyl chloride and acetone or benzophenone in ether was added to the magnesium covered by dry ether. The reaction temperature and the quantities of ether and magnesium were varied widely. Non-activated magnesium was used. In no case did either Reaction (I) or Reaction (II) occur.

The second series of experiments was also conducted according to Yavorsky's conditions, but the magnesium was initially activated with ethyl bromide. Sometimes the ethyl magnesium bromide was poured from the magnesium and replaced with dry ether, followed by addition of the ether solution of the myrtenyl chloride and the second component with stirring. At other times, the reaction was conducted without the removal of the ethyl magnesium bromide. In the experiments where the ethyl magnesium bromide was washed out, the yield of Reaction (I) (determined analytically by titration of the magnesium alcoholate with acid) approached zero with acetone and was about 30% with benzophenone.

Benzophenone and ethyl acetate were used as second components in the experiments where the ethyl magnesium bromide was not removed. In the case of benzophenone, the yield of Reaction (I) varied (the amount of ethyl magnesium bromide was taken into account) between 72-100%. Diphenylmyrtenylcarbinol was isolated as the reaction product (see Experimental; unsuccessful experiments are not reported). When the second component was ethyl acetate, the analytically determined yield was around 12%.

Apparently the yield of Reaction I under Yavorsky's conditions depends very much on the properties of the alcoholate of the tertiary alcohol that is formed. In the case of ethyl acetate, it rapidly precipitates from the solution as a sticky mass which covers the magnesium shavings and prevents any further reaction.

Repeated experiments in this direction showed that the chloride (A) reacts with magnesium activated by heating with 10% iodide to form up to 20% of $C_{10}H_{15}MgX$. When activated by coating with ethyl bromide (without removal of the C_2H_5MgBr), a yield up to 29% of $ClOH_{15}MgX$ was obtained. The yield in both cases was not constant, and depended upon the experimental conditions.

The activation causes the formation of some MgI_2 and $MgBr_2$ in the reaction medium, and cleans the surface of the magnesium. As was stated earlier, the chloroterpenes are allylic chlorides and easily take part in double decompositions. It was thought that when large amounts of $MgBr_2$ or MgI_2 were introduced into the reaction medium, the chloride (A) would be changed into the corresponding bromide or iodide, which would react more easily with the magnesium than the chloride. This hypothesis was verified. When the magnesium was initially treated with ether containing large amounts of bromine or iodine, it reacted with the chloride (A) almost completely. However, in the case of the bromine, the yield of Reaction (I) varied between 36-94%, depending on the amount of ether and on other factors. In the case of iodine, the yield did not exceed a certain percent because of the subsequent reaction according to Equation (II): $[C_{10}H_{15}MgI + C_{10}H_{15}I = (C_{10}H_{15})_2 + MgI_2]$.

In the interest of conciseness of this report, the results of the many separate experiments used to work out the final procedure are not given. Instead this procedure is given here: 30 g of dry bromine was slowly added, with cooling and mixing, to 50 g of magnesium turnings (not less than 99.8% pure; see below; 30-60 mesh) in 400 ml of dry ether (a round bottom flask with a reflux condenser, stirrer, and dropping funnel). After four hours of stirring at room temperature, a solution of 17 g of $C_{10}H_{15}Cl$ in 135 ml of dry ether was added. The stirring was continued for one hour more. An aliquot was removed and the yield of $C_{10}H_{15}MgX$ was determined by titration with 0.1 N acid in the presence of methyl orange (the yield usually was at least 70%). The $C_{10}H_{15}MgX$ solution was pumped over into another flask with dry nitrogen. The magnesium was washed twice with dry ether, covered with ether, and kept for the next experiment. The ether washes were added to the main solution. A triple adapter containing a stirrer, reflux condenser, and dropping funnel was attached and the second component was added.

When pure (> 99.8%) magnesium was used, the yield of the $C_{10}H_{15}MgX$ did not vary over a wide temperature range (+5 – +25°). When technical magnesium was used, the yield fell and varied with the temperature of the reaction medium. For example, with one sample of commercial magnesium containing iron, not more than 45% of the possible yield, and then only at temperatures of +10 – +13° was obtained. Over +20°, the yield dropped because of Reaction II, and below +10° the reaction was slow and incomplete.

The myrtenyl magnesium halide was reacted with carbon dioxide, acetone, acetaldehyde, orthoformic ester, acetyl chloride, and formaldehyde. In the last three cases the expected product was not obtained (homomyrtenal, methylmertenyl ketone, or methyldimyrtenyl ketone, and homomyrtenol). Instead complex mixtures, which did not give constant boiling fractions on rectification, were obtained. The first four cases gave the following (respectively): 1) dimyrtenyl ketone; 2) dimethylmyrtenylcarbinol; 3) methylmyrtenylcarbinol; 4) phenylmyrtenylcarbinol. Unsuccessful experiments are not reported in the experimental section. Diphenylmyrtenylcarbinol was obtained by Yavorsky's method. The unusual nature of the chemical properties of myrtenyl chloride and myrtenyl magnesium halides is fully illustrated by the above. Almost none of its possible reaction products can be obtained by the usual methods, and very often it is necessary to devise special methods in order to realize the desired reaction.

EXPERIMENTAL

Synthesis of diphenylmyrtenylcarbinol by Yavorsky's method. 1 g of ethyl bromide followed by a solution of 4.3 g of benzophenone, and the chloride (A) in 18 ml of ether were added to 5.6 g of magnesium covered with dry ether. It was then stirred for 14 hours without heating. Two runs were made. The yield of $C_{10}H_{19}MgHal$ was 72% of theory in both cases (allowing for C_2H_5MgBr). The reaction products in both cases were decomposed with 1% hydrochloric acid, the ether layer separated, and the ether distilled. The residue solidified. It may have contained traces of benzophenone (m.p. 48°) and diphenylethylcarbinol (m.p. 94-95°). The crystals were recrystallized from hot alcohol and then twice from ether; m.p. 172-178°.

Found %: C 85.3; H 6.5. $C_{33}H_{30}O$. Calculated %: C 86.7; H 8.2.

The substance was considered to be impure diphenylmyrtenylcarbinol. The wide melting point range also showed that this was an impure substance.

Myrtenyl magnesium chloride and carbon dioxide. Commercial dry ice was added to a solution of myrtenyl magnesium chloride in ether prepared from 17 g of the chloride (A) by the previously given method (74% yield). The reaction product was allowed to stand overnight and then worked up in the usual manner. α-Pinene was obtained as the main product. This indicated that the commercial dry ice contained water and that carbon dioxide reacted less readily with myrtenyl magnesium chloride than water.

In the next run (chloride (A) 18 g; yield of $C_{10}H_{19}MgHal$ 69%) a stream of dry carbon dioxide was passed into the ether solution of the Grignard reagent until the formation of the precipitate ceased. The reaction product was decomposed with hydrochloric acid, the ether layer separated, and distilled at 0.1 mm. Besides lower boiling fractions none of which titrated bases, a fraction of b.p. 120-125°, a sticky liquid, was obtained.

d_4^{20} 0.972; n_D^{20} 1.5143.

Found %: C 84.5, 84.7; H 10.2, 10.6. $C_{11}H_{18}O$ (Dimyrtenyl ketone). Calculated %: C 84.5; H 10.1.

In an alalogous run, 5.9 g of this fraction was obtained.

Myrtenyl magnesium halide and acetone. An ether solution of 11 g of acetone was added to an ether solution of $C_{10}H_{19}MgX$ obtained from 17 g of the chloride (A), and the flask was heated to reflux for one hour. The ether and the magnesium alcoholate were poured from the magnesium and shaken with water. The ether layer was separated, dried with powdered potassium hydroxide, poured from the hydroxide, and finally distilled at 0.1 mm through a small column. One fraction with a narrow boiling range throughout was obtained. This fraction had a b.p. of 69-71°.

d_4^{20} 0.977; n_D^{20} 1.50226; MR_D 58.7. $C_{12}H_{21}OH$. F □ Calculated 59.3.

Found %: C 80.4, 80.0, 80.0; H 11.4, 11.4, 11.7; OH 8.5, 8.3 (Tserevitinov). $C_{12}H_{21}OH$. Calculated %: C 80.3; H 11.4; OH 8.8.

Myrtenyl magnesium halide and acetaldehyde. Technical magnesium containing iron was used in this synthesis because of a temporary lack of pure magnesium. After a long search, the proper conditions for the preparation of $C_{10}H_{19}MgHal$ in a 30-40% yield were found. They are given below.

56 g of magnesium, 400 ml of ether, and 20 g of bromine were mixed together with ice cooling. 20 g of the chloride (A) in 150 ml of ether was then added over a 45 minute period. The temperature inside the flask was kept at 10-13° (cooled with ice water when necessary), while the mixture was stirred for 45 minutes. Then 5.2 g of acetaldehyde in 30 ml of ether was added over a 40 minute period. After being allowed to stand over-

night, it was worked up in the usual manner. 13.8 g of reaction product was obtained. It was distilled at 5 mm through a small column. Two constant boiling fractions were obtained: Fraction I, b.p. 83-85°, 2.6 g.

d_4^{20} 0.9775; n_D^{20} 1.4998; MR_D 54.14. $C_{12}H_{19}OH$ Calculated %: C 54.67.

Found %: C 77.2, 76.9; H 10.7, 10.5. $C_{12}H_{20}O$. Calculated %: C 80.0; H 11.1.

Fraction II, b.p. 135-140°, 5.5 g.

d_4^{20} 0.953; n_D^{20} 1.5142; MR_D 85.37. $C_{20}H_{30}$ Calculated 85.6.

Found %: C 87.4, 87.5; H 11.3, 11.1. $C_{20}H_{30}$. Calculated %: C 88.8; H 11.1;

This substance was dimyrtenyl.

Myrtenyl magnesium halide and benzaldehyde. Resublimed magnesium and 18 g of chloride (A) gave 81% of $C_{10}H_{17}MgHal$. An ether solution of 10 g of benzaldehyde was added to the above ether solution, separated from the magnesium, and the contents of the flask refluxed for one hour. Dilute acetic acid was then added until the precipitate dissolved, the ether layer was separated, washed with aqueous alkali, dried with powdered potassium hydroxide, poured from the hydroxide, and finally distilled through a small column at 2 mm. 6.3 g of a fraction with b.p. 140-146° was obtained. On redistillation (at 0.1 mm), it came over at 120-121° (5.6 g).

d_4^{20} 1.003; n_D^{20} 1.5321; MR_D 74.83. $C_{17}H_{21}OH$ Calculated: 74.16.

Found %: C 85.6, 85.2; H 9.4, 9.6. $C_{17}H_{22}O$. Calculated %: C 84.2; H 9.2.

SUMMARY

1. Myrtenyl chloride was used as a model to study the possibility for using the allylic chloroterpenes, initially obtained by the authors, in organo-magnesium syntheses.

2. It was shown that Yavorsky's method was feasible in isolated cases but could not be generally used.

3. Conditions were found for the preparation of individual myrtenyl magnesium halides in yields not less than 70%.

4. Myrtenyl magnesium halide was reacted with carbon dioxide, acetaldehyde, and benzaldehyde, with the expected products being obtained.

With ethyl acetate, ethyl orthoformate, acetyl chloride, and formaldehyde, the proper reaction conditions for the preparation of the normal products could not be found.

The results illustrate, once more, the qualitative unusualness of the behavior of the chloroterpenes.

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NEW TYPES OF TERPENE TRANSFORMATIONS

X. SYNTHESIS OF HOMOTERPENES

D. Tishchenko and V. Folladov

Homoterpenes result from the replacement of one or more hydrogen atoms of the terpenes by alkyl groups. Up to now they have been obtained by the reaction of organo-magnesium compounds with dihydroterpenyl aldehydes and ketones, followed by the removal of water from the secondary and tertiary dihydroterpenols that were formed. This method was used in a series of reactions by S. S. Nametkin and his students. However, it is not generally applicable, as the initial aldehydes and ketones are not always available, and may even be unknown. In addition, removal of water from the terpenol often leads to profound isomeric changes, so that the structure of the homoterpene obtained cannot be assigned only on the basis of the method of preparation.

Therefore, a method for the synthesis of the homoterpenes partly or entirely free from the above mentioned shortcomings was clearly desirable. Allylic chloroterpenes, obtained by the authors, contained replaceable chlorine atoms; for this reason, it was thought that they would easily react with organo-magnesium compounds to form homoterpenes:

$$C_{10}H_{15}Cl + ClMgR = C_{10}H_{15}R + MgCl_2.$$

It was shown previously (Communication IX) that the reaction between magnesium activated with iodine or bromine and the chloroterpenes was difficult to hold at the first level. Without the proper precautions, diterpenes are usually obtained in large amounts. Because of this, it could be considered that the authors' proposed synthesis of the homoterpenes was practical.

The equation cited above is only for the main reaction. It is well known that organo-magnesium compounds may act as reducing agents in a series of reactions, decomposing to an ethylenic hydrocarbon and HMgX. It is also quite clear that this reaction is between radicals, and that the free radicals R and R' can react among themselves to form R–R, R–R', and R'–R'. All of these reactions will lower the yield of the homoterpenes, and can be represented by the following equations:

$$C_2H_5CH_2MgX \longrightarrow CH_2{=}CH_2 + HMgX;$$
$$C_{10}H_{15}Cl + HMgX \longrightarrow MgXCl + C_{10}H_{16} \text{ (terpene)};$$
$$2C_{10}H_{15}Cl + 2C_2H_5CH_2MgX \longrightarrow 2MgClX + 2C_{10}H_{15}{-} + 2C_2H_5{-};$$
$$C_{10}H_{15}{-} + C_2H_5{-} \longrightarrow C_{10}H_{15}C_2H_5 \text{ (homoterpene)};$$
$$2C_{10}H_{15}{-} \longrightarrow C_{20}H_{30} \text{ (diterpenyl)};$$
$$2C_2H_5{-} \longrightarrow C_4H_{10} \text{ (butane)}.$$

According to the particular organo-magnesium compound used, terpene, diterpenyl, the new homoterpene, the ethylenic hydrocarbon, or bisalkane are obtained. All of these side products will lower the yield of the homoterpene.

The experimental results agree with the above equations: upon the addition of the chloroterpene to the ether solution of the organo-magnesium compound, a continuous stream of gas, which contained the ethylenic and bisalkane hydrocarbons, separated. In two cases, the ethylenic hydrocarbon was absorbed in bromine and the corresponding dibromoalkanes isolated. In all cases, lower boiling fractions containing the terpene corresponding to the chloroterpene were obtained. The diterpenyl was obtained in all cases. Nevertheless the yield of the desired product was fully acceptable in all cases and varied between 40 and 60%.

In order to ascertain the conditions for the synthesis of the homoterpenes, the reaction of 6-chlorodipentene with methyl, ethyl, n-propyl, and n-butylmagnesium halides was used and a series of 6-alkylditerpenes prepared. They are all liquids with reasonably pleasant odors. Their physical properties are listed in the table.

The structure of the homoterpenes as 6-alkyldipentenes was based on the conditions of the reaction. It is well known that organo-magnesium syntheses generally occur without isomerization.

Only the synthesis of *n*-propyldipentene is given in the experimental section, in order to conserve space. The other syntheses were effected in an analogous fashion.

EXPERIMENTAL

n-Propyl magnesium bromide was prepared from 5.0 g of magnesium and 29 g of propyl bromide in 50 ml of ether, in a round-bottomed flask with a reflux condenser, stirrer and dropping funnel. 20 g of 6-chlorodipentene in 30 ml of ether was then added to it with stirring. The gas which separated was collected (1370 ml). The flask was then heated to reflux for two hours, whereupon a crystalline precipitate of magnesium halide diethetate came out. 1200 ml of the gas was passed into bromine; 550 ml, i.e. 54%, was absorbed. The bromine was washed out of the dibromide with sodium sulfite and 4 g of a dense liquid boiling entirely at 140°, which corresponds to 1,2-dibromopropane, was obtained. The contents of the flask were ice-cooled, decomposed with water, and acidified to litmus with dilute nitric acid. 4.0 g of chloride ion was found in the water layer; a 90% reaction occurred. The ether was removed from the ether layer; weight of the residue, 20 g; it was distilled through a small column (4-5 theoretical plates) at 3 mm: the 1st fraction 58-68.5°, 0.75 g, d_4^{20} 0.855 contained chlorine; the 2nd fraction 68.5-82°, 0.70 g, d_4^{20} 0.850, contained chlorine; the 3rd fraction 82-85°, 9.1 g, d_4^{20} 0.858, n_D^{20} 1.4765, MR_D 58.65, $C_{13}H_{23}Cl$, calculated: 59.10, contained chlorine. The rest of the fractionation was done in a flask with a side tube at a pressure of about 0.001 mm: the 4th fraction, up to 60°, d_4^{20} 0.8524; the 5th fraction 60-118°, 0.4 g; the 6th fraction 118-125°, 3.9 g, d_4^{20} 0.920, n_D^{20} 1.5134.

1. Physical properties of the 6-alkyldipentenes

Alkyldipentene	Boiling point (in °C)	Pressure (mm)	d_4^{20}	n_D^{20}	ΣMR_D
$C_{10}H_{18}$	70-71	20	0.8436	1.4734	–
$C_{10}H_{15}CH_3$	74-76	14	0.8466	1.4748	+0.05
$C_{10}H_{15}C_2H_5$	46-47	0.75	0.8489	1.4760	+0.05
$C_{10}H_{15}C_3H_7$	56-57	0.4	0.8469	1.4755	+0.18
$C_{10}H_{15}C_4H_9$	79-80	1.3	0.8488	1.4757	+0.10

Found %: C 88.2; H 11.9; M 253, 252. $C_{20}H_{38}$. Calculated %: C 88.8; H 11.2; M 260.

Fractions 1 and 2 were combined, the mixture containing 0.35 g of chlorodipentene. The mixture was distilled at 762 mm. The main fraction boiled at 178-182°: d_4^{20} 0.851; n_D^{20} 1.4780; MR_D 45.28. $C_{10}H_{19}$. Calculated 45.24.

Fractions 3 and 4 were combined and allowed to stand with metallic sodium ribbon for three weeks, and then distilled at a pressure of about 0.4 mm. 7.0 g was distilled, yielding: 1st fraction, to 56.5°, 0.5 g; 2nd fraction, 56.5-57.5°, 5.85 g.

For the fraction with b.p. 56.5-57.5°, 5.85 g,

d_4^{20} 0.8469; n_D^{20} 1.4755; MR_D 59.284.
$C_{13}H_{23}Cl$. Calculated: 59.098. EMR_D + 0.186.
Found %: C 87.5, 87.3; H 12.6, 12.6. $C_{13}H_{24}$. Calculated %: C 87.55; H 12.45.

The yield of the second fraction (propyldipentene) was about 30%, for the other alkyldipentenes from 40 to 60%.

SUMMARY

1. A new method for the synthesis of homomoterpenes by the reaction of allylic chloroterpenes with organo-magnesium compounds is given. The yield of the alkylpentenes was from 30-60% of the possible. The side products obtained were an alkane, an alkene, a terpene, and a diterpenyl.

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BROMINATION WITH DIOXANE DIBROMIDE

I. THE BROMINATION OF PHENOLS

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The monobromination of phenols by the usual methods is a difficult task. It is almost impossible to obtain monobromophenols by direct bromination in acidic and neutral media: on shifting to basic media, the problem is further complicated by the concurrent oxidative processes. On brominating phenols in organic solvents such as glacial acetic acid, chloroform, carbon disulfide, etc., monobromo derivatives are obtained in certain cases (p- and o-bromophenol and bromohydroquinone). However, many especially polyhydric phenols (resorcinol, pyrocatechol, pyrogallol, and phloroglucinol) form the polybromo compounds at once. For these reasons the determination of a general method for the monobromination of phenol appeared to be an interesting problem. The literature contains several papers dealing with the monobromination of phenols. Thus in 1923 complex compounds of bromine and salts of pyridine, and quinoline (pyridine-dibromide hydrobromide, $C_5H_5NBr_2 \cdot HBr$) were used as brominating agents for the bromination of pyrocatechol, resorcinol, and pyrogallol [1]. The bromination with these reagents is effected in glacial acetic acid solutions at room temperature. Pyridine dibromide hydrobromide only monobrominates pyrocatechol; resorcinol and pyrogallol form dibromides. Monobromoresorcinol and monobromopyrogallol could only be obtained by using quinoline dibromide hydrobromide. It was recently shown that pyridine dibromide hydrobromide brominates 2-naphthol to 6-bromo-2-naphthol (yield 46.8%). It is interesting to point out that phenol, under the action of this reagent in [illegible] glacial acetic acid solution, forms tribromophenol instantly [2]. The main drawback in the method of bromination with the complex pyridine and quinoline bromides lies in the difficulty in isolating the monobromophenols from the reaction mixture, as many of them are extremely soluble in water and are very poorly extracted with the ether from the dilute aqueous acetic acid. These authors do not give any yields of the monobromophenols in most cases, and it is therefore difficult to judge the value of this method. N-Bromoacetamide [3] and N-bromosuccinimide [4] were used for the monobromination of phenols and certain phenolic ethers. Monobromo derivatives were obtained in all cases (phenol, anisole, phenetole, 3-methoxytoluene, 1,4-dimethoxybenzene, 1- and 2-methoxynaphthalene, and several others). However, the yields by this method were often very low: for example, for anisole, a 32% yield of p-bromoanisole; for phenetole, a 20% yield of p-bromophenetole; and for 3-methoxytoluene, a 49% yield of the 6-bromo derivative. Also, the reagents themselves cannot be considered common and readily available.

An interesting method of bromination by means of a mixture of dichlorourea and potassium bromide in a weakly acidic aqueous or nonaqueous medium, was proposed M. V. Likhosherstov [5]. However this method was not worked out in detail for phenols, the author only using it for the mono-, di-, and tribromination of phenol and resorcinol.

In the present paper are reported the results of using dioxane dibromide, recently proposed as a convenient means for the bromination of organic compounds [6], as a brominating agent for all phenols. Dioxane dibromide - a molecular compound of dioxane and bromine, composition $C_4H_8O_2 \cdot Br_2$ – was first reported by Favorsky [7]. Dioxane dibromide is very easily obtained by simply mixing equivalent amounts of dioxane and bromine in solvents (excess of dioxane, ether, dichloroethane, etc.) or without solvents. It is a light orange, crystalline substance, m.p. 86°. It has to be stored in glass stoppered jars or in sealed ampoules. Samples of dioxane dibromide can be stored for a long time without loss of activity. Dioxane dibromide is readily soluble in pyridine, dioxane, chloroform, dichloroethane, and carbon tetrachloride, and somewhat less soluble in ether.

When dioxane dibromide is first dissolved in ether, a transparent orange solution forms, but after some time the liquid becomes turbid and separates into two layers: a lower dark red, dense layer; and an upper transparent ether layer. The lower layer is insoluble in water, and rapidly forms a colorless solution containing bromide ions with alkali. The lower layer retains the brominating activity. The nature of this phenomenon

has not been studied further as yet. Dioxane dibromide is very poorly soluble in water. Water solutions of it gradually decompose in several days. The decomposition is more rapid when the water is boiled. It volatilizes in the air.

As a brominating agent, dioxane dibromide has many advantages in comparison to bromine and other brominating agents. It is extremely easy to prepare and very easy to weigh out; it is practically non-hazardous to work with, and is easily handled and stored.

The action of dioxane dibromide on monohydric phenols and their ethers was first studied. Phenol reacts extremely easily with dioxane dibromide. The reaction can be effected in ether and dioxane solutions, or without solvents. When one equivalent of phenol is used, monobromophenol is formed in all cases. It must be pointed out, however, that for the preparation of the para isomer, the reaction is best run in ether solution or without solvents, while cooling the reaction mixture with cold water. Significant amounts of the ortho isomer are formed without the cooling. When two or three equivalents are used for the bromination, the excess dioxane dibromide does not react, and the only reaction product is monobromophenol.

Anisole, analogously to phenol, is brominated very easily in the cold to p-bromoanisole. In this case, the bromination can also be effected either in ether or without solvents. With other phenols, thymol is brominated to 4-bromothymol, and 1,3,5-xylenol to 4-bromo-1,3,5-xylenol. The yields of the monobrominated products are from 75 to 95%.

The dihydric phenols, hydroquinone, resorcinol, and pyrocatechol are readily brominated by dioxane dibromide. The bromination is more expedient when run in ether solution. It must be pointed out that monobromopyrocatechol and monobromoresorcinol are extremely difficult to crystallize. Crystalline products are only formed after the oil obtained initially is allowed to stand for long periods of time in a vacuum desiccator over sulfuric acid. However, once crystallized, the products behave normally and can easily be recrystallized from petroleum ether. K. Rosenmund [1] and N. V. Likhosherstov [5] also mention the difficult crystallization of 4-bromoresorcinol and 4-bromopyrocatechol. Apparently the difference between these compounds and the closely related bromohydroquinone can be explained by the contamination of 4-bromoresorcinol and 4-bromopyrocatechol by slight traces of other possible isomers. Besides the above, other dihydric phenols, orcin and guaiacol were also brominated. Orcin forms 2-bromoorcin in a 90% yield. Guaiacol – 5-bromoguaiacol.

The use of two or more equivalents of dioxane dibromide for the bromination of the dihydric phenols, as for example hydroquinone, leads to the formation of dibromohydroquinone; higher brominated products are not formed.

The monobromination of the trihydric phenols has been the least studied. Only the monobrominated derivative of pyrogallol is known. Only tribromo derivatives were obtained from phloroglucinol and hydroxyhydroquinone. The action of dioxane dibromide on the simplest of the trihydric phenols, pyrogallol, hydroxyhydroquinone, and phloroglucinol, was studied. The bromination of pyrogallol is the smoothest, giving excellent yields of 4-bromopyrogallol or 4,6-dibromopyrogallol depending on the quantity of dioxane dibromide used. A strong darkening occurs on the bromination of hydroxyhydroquinone even in dilute ether solutions at 0°. No definite products could be isolated from the dark brown reaction mixture. Apparently in this case, along with the bromination, a simultaneous oxidation of the hydroxyhydroquinone, which is particularly unstable to oxidation, occurs.

In contrast to hydroxyhydroquinone, phloroglucinol brominates very smoothly, the use of one or two equivalents of the reagent leading to the formation of only one product, which, according to its bromine content, is dibromophloroglucinol. This compound was previously unreported. Whether or not phloroglucinol reacts in this case as a phenol or in its tautomeric carbonyl form, is not clear; this question needs further study. Dibromophloroglucinol is very soluble in ether, alcohol, and other common organic solvents; it is poorly soluble in cold water, and is crystallized from boiling water in the form of fine needles, m.p. 146°.

The action of dioxane dibromide on certain naphthols and hydroxyphenanthrenes was also studied. 1-Naphthol, 2-naphthol, and nerolin brominate well with dioxane dibromide in dioxane solution to form the respective 4-bromo-1-naphthol, 1-bromo-2-naphthol, and 1-bromonerolin in high yield.

The bromination of the hydroxyanthraquinones was somewhat more difficult. 1-Hydroxyanthraquinone, 2-hydroxyhydroquinone, 1,2-dihydroxyanthraquinone (alizarin), and 1,5-dihydroxyanthraquinone (anthrarufin) were brominated. To produce the monobromo derivatives, it was necessary to heat an equivalent molecular

mixture of the components to 50-60° for a short time. Analogous to the hydroxyanthraquinones, the bromination of phenols with a negative substituent-nitrophenol, salicylic acid – was done by heating to 50-60°. These compounds form only monosubstituted products even with large excesses of the reagent.

EXPERIMENTAL

Preparation of dioxane dibromide. 500 g of redistilled dioxane was placed in a 2-liter porcelain beaker, and 990 g (317 ml) of bromine was rapidly added with stirring and cooling with ice water. The hot dark brown solution obtained was poured with stirring into 2 liters of ice and water. A crystalline orange precipitate formed. It was filtered, pressed carefully, first on the filter, and then to dryness on a porous plate. The yield of dioxane dibromide was 1400 g (94%) m.p. 60°.

Bromination of phenol. 25 g of dioxane dibromide was added in small portions with shaking and water cooling to 9.4 g of crystalline phenol. The mixture liquified and HBr was given off. After the addition of all of the reagent, the mixture was poured into water and extracted with ether. The ether extract was dried with calcium chloride, and, after removal of the ether, was vacuum distilled. 15 g (88%) of p-bromophenol was obtained; b.p. 115-117° at 11-12 mm; m.p. 64-65°.

Bromination of anisole. 10.8 g of anisole was brominated with 25 g of dioxane dibromide in a manner analogous to phenol. The reaction mixture was washed with dilute sodium hydroxide solution and water; the oil separated, dried with calcium chloride, and vacuum distilled. 10.7 g (57%) of p-bromoanisole was obtained, b.p. 99-100° at 18 mm; n_D^{20} 1.5631.

Bromination of thymol (1-hydroxy-3-methyl-6-isopropylbenzene). 8.3 g of dioxane dibromide was added with shaking to 5 g of thymol dissolved in 10 ml of dioxane. The mixture was poured into water and extracted with ether. The ether extract was dried with anhydrous magnesium sulfate and the ether evaporated. The residual oil crystallized after standing in a vacuum desiccator over sulfuric acid. 7 g (90%) of 4-bromothymol (4-bromo-1-hydroxy-3-methyl-6-isopropylbenzene) was obtained, m.p. 55-56° (from petroleum ether).

Bromination of 1,3,5-xylenol. 12.2 g of xylenol was dissolved in ether and brominated with 25 g of dioxane dibromide. After addition of all of the reagent, the mixture was washed with water and dried with anhydrous magnesium sulfate. After removal of the ether, it was vacuum distilled. 15 g (75%) of 4-bromo-1,3,5-xylenol was obtained, b.p. 116-118° at 18-20 mm; m.p. 54°.

Bromination of hydroquinone. a) An ether solution of 5 g of dioxane dibromide was dropped with shaking and cooling into 2.2 g of hydroquinone dissolved in ether. The transparent solution obtained was washed with water, dried with calcium chloride, and the ether evaporated. 3.4 g (90%) of bromohydroquinone was obtained; m.p. 109° (before recrystallization), m.p. 110-111° (from n-heptane). b) 2.2 g of hydroquinone in ether was brominated with 10 g of dioxane dibromide. 4.82 g (90%) of 2,6-dibromohydroquinone was obtained; m.p. 164° (before and after recrystallization from water).

Bromination of pyrocatechol. A solution of 25 g of dioxane dibromide in 50 ml of ether was added with shaking to 11 g of pyrocatechol dissolved in 50 ml of ether. The mixture was washed several times with water, dried with anhydrous magnesium sulfate, and freed from the ether. The thick lightly colored oil obtained crystallized after a prolonged stay in a vacuum desiccator over sulfuric acid. 17 g (85%) of 4-bromopyrocatechol was obtained; m.p. 82° (before recrystallization), 86-87° (from petroleum ether).

Bromination of resorcinol. a) 1.1 g of resorcinol in 15 ml of ether was brominated by 2.5 g of dioxane dibromide in 20 ml of ether. The lightly colored mixture obtained was washed with a sodium sulfite solution and water, dried with anhydrous magnesium sulfate, and the ether evaporated. The residual oil crystallized only after a prolonged stay in a vacuum desiccator over sulfuric acid. 3.7 g (97%) of 4-bromoresorcinol, m.p. 101-102°, was obtained. b) 1.1 g of resorcinol in 20 ml of water was brominated with 4.96 g of dibromo dioxane. 2.48 g (93%) of 4,6-dibromoresorcinol was obtained, m.p. 110-112° (from water).

Bromination of orcin (2,6-dihydroxytoluene). 3.2 g of orcin in ether solution was brominated with 5.2 g of dioxane dibromide. The mixture was washed with water, dried with anhydrous magnesium sulfate, and the ether evaporated. The residual oil rapidly crystallized in vacuum desiccator over sulfur acid. 4 g (90%) of 2-bromo-orcin (2-bromo-3,5-dihydroxytoluene) was obtained; m.p. 134-135°.

Bromination of guaiacol (1-methoxy-2-hydroxybenzene). 12.6 g of guaiacol in ether was brominated with 25 g of dioxane dibromide. After washing, drying, and ether distilling, the residue was vacuum distilled. 18 g

(88%) of 5-bromoguaiacol (5-bromo-2-methoxy-2-hydroxy-benzene) was obtained: b.p. 170-174° at 15-18 mm; m.p. 44-45° (from petroleum ether).

Bromination of pyrogallol. a) 1.26 g of pyrogallol was brominated in ether with 2.5 g of dioxane dibromide. After processing in the usual manner and evaporating the ether, 1.95 g (95%) of 4-bromopyrogallol was obtained; m.p. 140° (decomp.). b) 1.26 g of pyrogallol in ether solution was brominated with 5 g of dioxane dibromide. 2.64 g of dibromopyrogallol was obtained, m.p. 149-150° (from benzene).

Bromination of phloroglucinol. 1.26 g of phloroglucinol was brominated in ether solution with 5 g of dioxane dibromide. After working up in the usual manner, 2.7 g of dibromophloroglucinol was obtained, m.p. 146 (from water).

8.550 mg substance: 4.763 mg Br (combustion in a stream of O_2). 5.300 mg substance: 2.965 mg Br, Found %: Br 55.70, 55.94, $C_6H_4O_3Br_2$. Calculated %: Br 56.29.

Bromination of 1-naphthol. 1.44 g of 1-naphthol in 20 ml of dioxane was brominated with 2.48 g of dioxane dibromide. 1.7 g (78%) of 4-bromo-1-naphthol was obtained; m.p. 112° (from aqueous methanol).

Bromination of 2-naphthol. 7.2 g of 2-naphthol was brominated in an analogous manner to 1-naphthol with 12.5 g of dioxane dibromide in dioxane solution. 10 g (90%) of 1-bromo-2-naphthol was obtained; m.p. 82° (from aqueous methanol).

Bromination of nerolin (2-methoxynaphthalene). 1.47 g of nerolin was brominated in dioxane solution with 2.5 g of dioxane dibromide. 2.3 g (97%) of 1-bromo-2-methoxynaphthalene was obtained; m.p. 83-84° (from aqueous methanol).

Bromination of 1-hydroxyanthraquinone. Several milliliters of dioxane were added to 2.24 g of 1-hydroxyanthraquinone and 2.5 g of dioxane dibromide, which had been carefully mixed together, and the mixture heated for 10 minutes to 50-60°. The mixture was poured into water, the precipitate filtered, and air dried. 2.99 g of 4-bromo-1-hydroxy-anthraquinone was obtained, m.p. 197° (from glacial acetic acid).

Bromination of 2-hydroxyanthraquinone. 2.24 g of 2-hydroxyanthraquinone was brominated in an analogous manner to 1-hydroxyanthraquinone with 2.5 g of dioxane dibromide. 2.8 g of 1-bromo-2-hydroxy-anthraquinone was obtained, m.p. 187° (from methanol).

Bromination of 1,2-dihydroxyanthraquinone (alizarin). 1.2 g of alizarin was carefully mixed with 1.25 g of dioxane dibromide and the mixture was heated to 50-60°, whereupon the color changed from orange-yellow to brown. The pasty mass obtained was worked up with sodium carbonate solution, acetic acid, and water, filtered, and air dried. Yield 1.6 g (100%); m.p. 264° (decomp.) (from aqueous acetic acid).

Bromination of salicylic acid. 6.9 g of salicylic acid mixed with 12.5 g of dioxane dibromide was heated to 70°. The colorless mixture was poured into water. 9.6 g of 4-bromosalicylic acid was obtained; m.p. 164-165° (from water.).

Bromination of 4-nitrophenol. 4.6 g of 4-nitrophenol was brominated in an anologous manner to salicylic acid with 8.3 g of dioxane dibromide. The mixture was poured into water, the precipitate separated and dissolved in methanol. A crystalline product was obtained by slowly evaporating the alcohol. 6 g (82%) of 2-bromo-4-nitrophenol was obtained; m.p. 112-114°.

SUMMARY

A new method is given for the bromination of phenols, naphthols, and hydroxyanthraquinones with the addition product of bromine and dioxane — dioxane dibromide.

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BROMINATION WITH DIOXANE DIBROMIDE

II. THE BROMINATION OF ALDEHYDES AND KETONES

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The direct bromination of aldehydes and ketones, as a rule, gives poor results, as the hydrogen bromide generated catalyzes the polymerization and condensation processes, especially for the aldehydes. The aldehydes are immediately changed by the action of acids into acidophobic compounds, such as the five membered heterocycles, pyrans and pyrroles. Ketones are much more stable to acids; however, many of them are strongly colored by the direct action of bromine. Because of this, there are no general and simple methods for brominating carbonyl compounds up to the present time.

All of the previous methods for the preparation of α-bromaldehydes do not start with the free aldehydes. The methods can be separated into two groups. The first group uses polymers of the aldehydes, such as paraldehyde. These trimers are brominated with bromine in carbon disulfide [1], or without solvents at low temperatures, −10-15° [2], and the bromo trimeric derivatives are depolymerized by heating to 140-160°. It must be pointed out, however, that the methods based upon the above principles nearly always give poor yields of the bromaldehydes (20-25%). The second group consists of methods which use monomers − aldehydes with protected carbonyl groups. The best worked out methods are those which use phosphorus trichlorodibromide, PCl_3Br_2, to brominate acetals [3]. A recently proposed method for the preparation of α-bromaldehydes uses enolacetates, which are reacted with bromine and then saponified [4]. The main fault of this group of methods is their length and many steps. Also, the yield of the final product leaves much to be desired. The yield does not exceed 40-45%, calculated on the aldehyde used.

As has been stated above, the direct bromination of ketones is possible. However, here the reaction is often complicated by a series of side reactions: oxidation, condensation, and polymerization. Many ketones can be advantageously brominated by a method worked out by A. E. Favorsky [5] in the presence of calcium carbonate. A rather good brominating agent for aliphatic ketones, starting with acetone, is PBr_5, as first shown by Favorsky[5]. Recently pyridinedibromide-hydrobromide [6] has been proposed as a brominating agent for ketones, especially those of the sterol series. N-bromsuccinimide [7] has also been used for the bromination of certain ketones.

In spite of the large number of proposed methods, not one of these can be used generally. Besides, the brominating agents are not always available, nor the method convenient, nor the yield of the bromoketone good.

In this report the results of the work on the use of dioxane dibromide as a brominating agent for aldehydes and ketones is given [8].

It was found that dioxane dibromide is an excellent brominating agent for both the aliphatic and alicyclic aldehydes and ketones. The bromination proceeds rather easily in the cold, and is not accompanied by polymerization or oxidation. The bromination may be made without solvents, but the best results are obtained in dioxane or ether solutions, especially in the latter. When the reaction is run in ether, very often two layers are formed in the reaction mixture. The upper, as the experiment showed, consisted of the bromaldehyde and the unreacted aldehyde in ether solution. The lower layer − a thick oil, which darkened in the air − is very soluble in water. The bromide ion is found in the aqueous solution. Upon making the aqueous solution basic, a distinct odor of dioxane is noticed. Apparently the lower layer is nothing more than a solution of hydrogen bromide in dioxane or, perhaps, even the unstable dioxanebromohydrin. This convenient separation of the hydrogen bromide from the reaction sphere results in a full protection of the aldehydes and ketones remaining in the ether from its harmful effects.

The yield of the brominated aldehydes and ketones in most cases is sufficiently high. Low yields were obtained for bromacetaldehyde (25-30%), phenylbromacetaldehyde (35-40%), and bromodecylaldehyde (20-25%); the latter was never obtained in an analytically pure state. However, the low yields did not arise from processes

occurring during the bromination, but from the inherent instability of the compounds themselves. Bromacetaldehyde, as is evident from the literature [9], rapidly polymerizes. Phenylbromacetaldehyde and bromodecylaldehyde decompose strongly on vacuum distillation, with the cleavage of HBr.

The proposed method was found especially convenient for alicyclic ketones which do not give good results with the other methods. This method was used in Acad. A. N. Nesmeyanov's laboratory for the bromination of spiro-4,5-decanon-6, 7-methylspiro-4,5-decanon-6, and 2,2,6-trimethylcyclohexanon-1; in all cases the corresponding α-bromoketones were obtained in high yields (50-80%).

The action of dioxane dibromide was studied on nine aldehydes: acetaldehyde, propionaldehyde, butyraldehyde, isobutyraldehyde, isovaleraldehyde, heptaldehyde, octylaldehyde, decylaldehyde, and phenylacetaldehyde; and on seven ketones: acetone, dipropyl ketone, diisopropyl ketone, cyclohexanone, menthone, acetophenone, and camphor.

It is interesting to point out that different types of camphor react differently with dioxane dibromide. For example: Japanese camphor starts reacting after the reaction mixture is heated for two minutes on the burner; native (Siberian) camphor reacts after several seconds of heating; while synthetic camphor only reacts after being heated for 10-15 minutes on the burner. However, camphor appears to be the only ketone among those studied which requires heating for the reaction.

EXPERIMENTAL

Bromination of acetaldehyde. 50 g of dioxane dibromide dissolved in ether was added dropwise at 5-10° to a solution of 8.8 g of acetaldehyde in 50 ml of ether. After the decolorization of the mixture, it was washed with a small amount of water, aqueous sodium carbonate, again with water, dried with anhydrous magnesium sulfate, the ether carefully removed, and the residue distilled. 7.5 g of bromacetaldehyde, b.p. 104-105°, n_D^{20} 1.4790, was obtained.

Bromination of propionaldehyde. 25 g of dioxane dibromide was added in small portions with shaking and water cooling to 5.8 g of the aldehyde dissolved in 25 ml of ether. The first portion of the reagent decolorized in 4-5 minutes, the later portions decolorized immediately. At the same time the solution darkened and separated into layers. At the end of the reaction, the lower layer was separated and the upper layer washed thoroughly with water, separated, and distilled. 7 g (51%) of the α-bromopropionaldehyde was obtained; b.p. 109-110°; n_D^{20} 1.4818.

Bromination of butyraldehyde. 50 g of dioxane dibromide was added with water cooling and stirring to 14.4 g of butyraldehyde. 2-3 minutes after addition of all of the reagent the mixture decolorized completely. The mixture was poured into water, the oil which separated taken up in ether, the ether layer washed and dried; after removal of the ether, the residue was vacuum distilled. 20.5 g of α-bromobutyraldehyde (68%) was obtained; b.p. 68-70° at 35-40 mm; n_D^{20} 1.4688.

Bromination of isobutyraldehyde. 7.2 g of isobutyraldehyde was brominated with 25 g of dioxane dibromide in ether solution. The decolorization of the reagent occurred very rapidly and the mixture separated into layers. After the usual workup, 9 g (58%) of α-bromoisobutyraldehyde was obtained; b.p. 112-113°; n_D^{20} 1.4530.

Bromination of isovaleraldehyde. 8.6 g of isovaleraldehyde was brominated in ether solution with 25 g of dioxane dibromide in the usual manner. 14 g (89%) of α-bromoisovaleraldehyde was obtained; m.p. 46-47° at 15 mm; n_D^{20} 1.4622.

Bromination of heptaldehyde. 25 g of dioxane dibromide was added in small portions, with water-cooling and shaking, to 11.4 g of freshly distilled heptaldehyde; after each addition, we waited until the reaction mixture was completely decolorized before adding the next portion of the reagent. At the beginning, a rapid decolorization occurred, the last portions of the reagent decolorized slowly. At the end of the reaction there was a slight darkening and a separation of layers. The lower layer was separated, the upper taken into ether, washed very thoroughly with water, and dried with anhydrous magnesium sulfate. The ether was evaporated in vacuo and the residue was then rapidly distilled in a stream of nitrogen. 12 g (62%) of α-bromoheptaldehyde was obtained: b.p. 78-80° at 10 mm; n_D^{20} 1.4650.

Bromination of octaldehyde. 12.8 g of freshly distilled n-octaldehyde was brominated in ether (25 ml) solution with 25 g of dioxane dibromide, the reagent being added stepwise with water cooling and shaking, and with waiting each time for the complete decolorization. At first the reagent decolorized slowly, then extremely

rapidly; the final portions of the reagent decolorized slowly. The mixture separated into layers. It was processed in the same way as heptaldehyde. 11.4 g (55%) of α-bromoctaldehyde was obtained; b.p. 110-111° at 23 mm; n_D^{20} 1.4650.

8.690 mg substance: 14.710 mg CO_2; 5.767 mg H_2O; 3.380 mg Br 5.380 mg substance: 9.130 mg CO_2; 3.825 mg H_2O; 2.235 mg Br. Found %: C 46.20, 46.31; H 7.43; Br 38.89, 38.80. $C_8H_{15}OBr$. Calculated %: C 46.17; H 7.27; Br 38.40.

This was the first preparation of α-bromoctaldehyde.

Bromination of decaldehyde. 15.6 g of freshly distilled n-decaldehyde was brominated with 25 g of dioxane dibromide in ether solution in the same manner as for n-octaldehyde. After processing it in the usual manner, the ether was evaporated in vacuum and the residue vacuum-distilled in a stream of nitrogen. In spite of all precautions, a strong decomposition took place during the distillation with the separation of HBr. A fraction collected at 120-130° at 14-16 mm, yellowish brown in color, was redistilled. On redistillation a decomposition and separation of HBr again occurred. 5 g of a light yellow liquid with lachrymatory properties was obtained, b.p. 128-130° at 15 mm; the liquid darkened rapidly. The bromodecaldehyde could not be obtained in an analytically pure state. The action of phenylhydrazine on either an alcohol or ether solution of the brominated aldehyde produced the cleavage of hydrogen bromide and the formation of phenylhydrazine hydrobromide, with separation of a thick oil, which did not have lachrymatory properties and contained no bromine. The action of sodium bisulfite on the brominated aldehyde did not lead to the formation of a definite product.

Bromination of phenylacetaldehyde. 12 g of freshly distilled phenylacetaldehyde was brominated in the usual manner in an ether solution. After the standard work up, the bromaldehyde obtained was vacuum-distilled in a stream of nitrogen. 8 g (40%) of phenylbromacetaldehyde was obtained; b.p. 112-114° at 15 mm; n_D^{20} 1.5916.

Bromination of acetone*. 11.6 g of acetone was brominated in ether solution with 50 g of dioxane dibromide, with shaking and water cooling. The colorless solution was well washed with water, sodium carbonate solution, again with water, and dried with anhydrous magnesium sulfate. After the removal of the ether, the residue was vacuum-distilled in a stream of nitrogen. 22.8 g (83%) of bromacetone was obtained; b.p. 44-46° at 15 mm. The whole process must be carried out the same day, without postponing the distillation, or the yield drops sharply.

Bromination of dipropyl ketone. 25 g of dioxane dibromide was slowly added to 11.7 g of dipropyl ketone. A rapid decolorization and a slight warming of the reaction mixture occurred. The reaction mixture was poured into water and the oil which separated taken into ether, washed, dried, and distilled. 15 g (78%) of the bromoketone was obtained; b.p. 78-80° at 15 mm.

Bromination of diisopropyl ketone. 25 g of dioxane dibromide was added in small portions to 11.2 g of diisopropyl ketone dissolved in 10 ml of dioxane. Within 2-3 minutes after the addition of all the reagent, the mixture decolorized. The solution was poured into water, the oil separated, dried, and vacuum-distilled. 15 g (78%) of the bromodiisopropyl ketone was obtained: b.p. 152-153° at 11 mm; n_D^{20} 1.4512.

Bromination of menthone. 8 g of menthone was brominated in a dioxane solution in analogous fashion, with 13 g of dioxane dibromide. After the usual processing, it was vacuum-distilled in a stream of nitrogen. 7 g (59%) of bromomenthone was obtained; b.p. 102-105° at 14 mm.

Bromination of cyclohexanone. 10 g of cyclohexanone was brominated in a dioxane-ether mixture (10 ml + 50 ml) with 25 g of dioxane dibromide. The mixture was thoroughly washed with water, dried, and vacuum-distilled in a stream of nitrogen. 11 g (60%) of bromocyclohexanone was obtained; b.p. 114-116° at 32 mm.

Bromination of acetophenone. 11 g of acetophenone was brominated in dioxane solution with 25 g of dioxane dibromide. The mixture was poured into water, the oil taken up into ether, dried and the ether evaporated.

* It must be pointed out that if the acetone contains alcohol or other contaminants, the start of the reaction is delayed. In this case it is desirable to add a drop of conc. hydrochloric acid to the mixture, and to warm it up slowly. As soon as the first portion of the reagent is decolorized, the subsequent portions are decolorized immediately.

The residue crystallized on standing. 18 g (95%) of ω-bromacetophenone was obtained: m.p. 50° (from aqueous methanol).

Bromination of camphor. 4.5 g of Japanese d-camphor was mixed with 7.5 g of dioxane dibromide and and heated for 2-3 minutes on the burner. The mixture decolorized with the separation of HBr. It was poured into water; the oil which separated crystallized rapidly. The crystals were sucked off and air dried. 5.6 g (80%) of d-bromocamphor was obtained, m.p. 74° (before recrystallization), 75° (from aqueous alcohol).

SUMMARY

A new method of brominating aldehydes and ketones by means of dioxane dibromide is given.

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STERIC HINDRANCES IN ORGANO-MAGNESIUM REACTIONS

XIV. AN UNUSUAL REACTION BETWEEN α-MONOCHLOROETHERS AND ARYL MAGNESIUM HALIDES

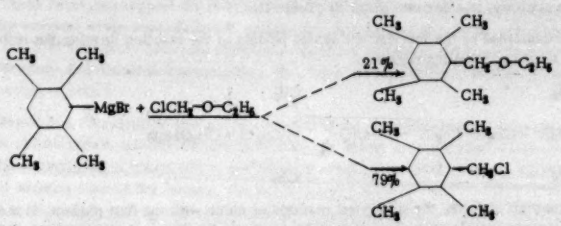
I. I. Lapkin and O. M. Lapkina

In a previous communication [1], it was shown the reaction of aryl magnesium halides with monochloromethylalkyl ethers, in relation to the degree of orthosubstitution of the phenyl radical by the alkyl groups, leads to different results. Unsubstituted and orthomonosubstituted aryl magnesium halides, as well as naphthyl magnesium halides, react normally with the above ethers to give the corresponding ether. When orthodisubstituted aryl magnesium halides react with the same monochloromethylalkyl ethers, the character of the reaction changes and the main product of the reaction is not the corresponding ether, but the orthodisbustituted benzyl chloride.

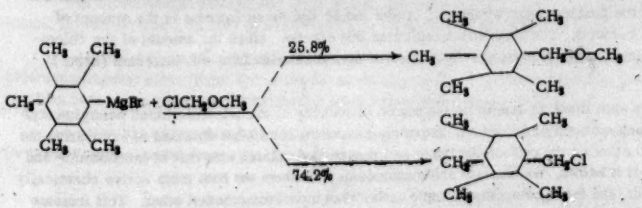
In the same report it was stated that the reason for this reaction path lies in the fact that, in the presence of the ortho effect on phenyl radicals, the sterically more accessible, although less reactive, alkoxy group of the chloroether reacts, instead of the more reactive chloromethyl group.

In order to confirm the unusual reaction between the above substances, two more reactions, the reaction of duryl magnesium bromide and monochloromethylethyl ether and the reaction between pentamethylphenyl magnesium bromide and monochlorodimethyl ether, were studied.

The first reaction, under the conditions used (Expt. 1), led to the formation of the following products:



The second reaction under analogous conditions (Expt. 2) gave the following products:



In order to be satisfied that the conclusion given on the reasons for the unusualness of the above reaction was correct, it was necessary to examine all variations in the mechanism of this anomaly.

First of all it was necessary to examine the possibility of the formation of the orthodisubstituted benzyl chlorides as a consequence of the easy hydrolysis of α-chloroethers. The HCl formed on hydrolysis could have split the benzylalkyl ether — the normal reaction product — forming, in this way, the benzyl chloride.

$$R\text{-}CH_2\text{-}O\text{-}CH_3 + HCl \longrightarrow R\text{-}CH_2OH + CH_3Cl;\ R\text{-}CH_2OH + HCl \longrightarrow R\text{-}CH_2Cl + H_2O.$$

TABLE 1

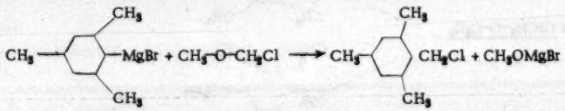
Reaction components (ratio 1:1)	Duration of heating, in hours	Composition of the reaction product (in %)	
		2,4,6-Trimethylbenzylmethyl ether (by calculation)	2,4,6-Trimethylbenzyl chloride
1. Mesityl magnesium bromide + monochloromethyl ether	1	38.0	62.0
2. Ditto	3	42.1	57.9
3. Ditto	5	45.2	54.8

TABLE 2

Reaction components	Ratio of the reaction components	Composition of the reaction product (in %)	
		2,4,6-Trimethylbenzylmethyl ether (by calculation)	2,4,6-Trimethylbenzyl chloride
1. Mesityl magnesium bromide + monochloromethyl ether	1:0.75	49.5	50.5
2. Ditto	1:1	38.2	61.8
3. Ditto	1:1.25	30.7	69.3

This equivalent variation of the reaction mechanism, however, had to be excluded because: first, the reaction was run under conditions which prevented the entrance of moisture into the flask; secondly, if the formation of the benzyl chlorides depended on the hydrolysis of the monochloromethylalkyl ethers, then it should have been formed in the case of the orthomonosubstituted benzylalkyl ethers, which, however, as the experiment proved, did not occur. Besides, if the process which formed the benzyl chloride was a secondary process, then an increase of the heating period would have increased the amount of the benzyl chloride in the reaction mixture, which actually, did not happen. Special experiments proved that increasing the heating period of the reaction mixture was not accompanied by an increase in the amount of benzyl chloride in the reaction products, but, on the contrary, in a decrease (Expt. 3) (Table 1).

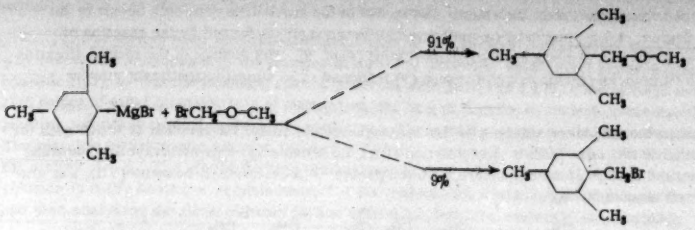
This decrease may be explained by the fact that the second product of the reaction forming the orthodisubstituted benzyl chloride as in the following equation:



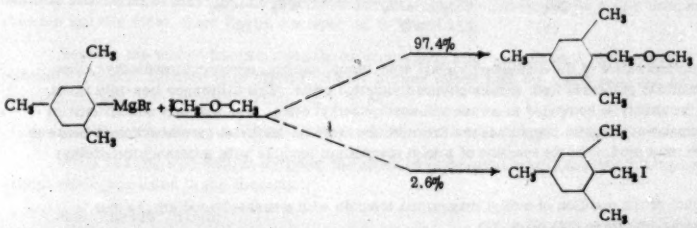
appears to be the alkoxy magnesium bromide, the subsequent reaction of which with the first product, is the reason for the formation of a certain amount of the benzylalkyl ether. From this fact it also follows that if the reaction is run with an excess of monochloromethyl ether, which reacts more rapidly with the alkoxy magnesium bromides, then the yield of the product ought to increase. There should also be an increase in the amount of benzyl chloride in the total products. The experiment confirmed this exactly. When the amount of the chloroether was increased, the amount of the product and the amount of benzyl chloride in it was increased (Expt. 3) (Table 2).

Finally, experiments were made to determine the degree of stability of the orthosubstituted benzylmethyl ethers to the action of monochloromethylethyl ether. Extremely interesting results are obtained on comparing the action of monochloromethyl ether on the orthodisubstituted aryl magnesium halides with that of monobromo- and monoiodomethyl ether. As it is known, monobromo- and monoiodomethyl ethers are both more active chemically than monochloromethyl ether, and monoiodomethyl is more active than monobromomethyl ether. This increase in chemical activity of the bromo- and iodoethers overcomes the steric hinderance of the alkyl orthosubstituents and because of this, the reaction between the orthodisubstituted aryl magnesium halides and the above haloethers has a different character.

The main reaction product from the reaction of monobromomethyl ether with mesityl magnesium bromide appears to be methyl-2,4,6-trimethylbenzyl ether. The second reaction product, 2,4,6-trimethylbenzylbromide is obtained in insignificant quantity (Expt. 4).



Monoiodomethyl ether reacts even more actively with mesityl magnesium bromide. The main product of the reaction appears to be methyl-2,4,6-trimethylbenzyl ether, the amount of 2,4,6-trimethylbenzyl iodide in the reaction product is even less. (Expt. 5).



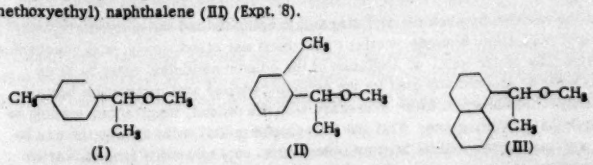
These facts also support the conclusion that the reason for the anomalous course of the reaction studied lies in the unequal steric accessibility of groups, and that the synthesis of the orthodisubstituted benzyl chlorides is not a result of secondary processes (hydrolysis, terminal cleavage), because these processes are more pronounced for monobromo- and monoiodomethyl ethers, and the reaction with these substances takes a normal course with the formation of ethers.

There is a considerable interest in the study of the reaction between the same organo-magnesium compound and other chloro ethers, namely the α-chloroethylalkyl ethers. A comparison of the activity of the α-halide found in the chloromethylalkyl ethers and in α-chloroethylalkyl ethers, shows that the halide in the latter has a greater degree of activity than in the former. For this reason the α-haloethylalkyl ethers which contain a halogen atom attached to secondary carbon react more readily than the halomethyl alkyl ethers in which this atom is found attached to a primary carbon atom.

The orthomonosubstituted and unsubstituted aryl magnesium halides react with α-monochloroethylalkyl ethers, as was expected, mainly in the direction of the formation of ethers.

1-Methyl-4-(α-methoxyethyl)benzene (I) is formed by the reaction of p-tolyl magnesium bromide with α-chloroethylmethyl ether (Expt. 6). A similar product, 1-methyl-2-(α-methoxyethyl)benzene (II) is formed by the reaction between α-monochloroethylmethyl ether and o-tolyl magnesium bromide (Expt. 7).

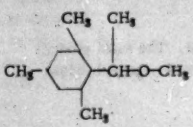
α-Naphthyl magnesium bromide also reacts normally with the above ether, i.e. with the formation of 1-(α-methoxyethyl) naphthalene (III) (Expt. 8).

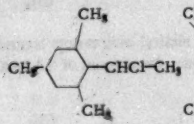


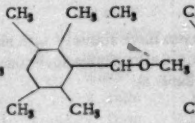
Of the two possible directions for the reaction with orthodisubstituted aryl magnesium halide which (the directions) were discussed above, the first proved to be the main one. The main products of the reaction were,

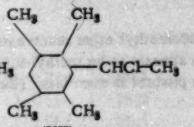
as in the case of the orthomonosubstituted, the ethers. The second of the above directions only occurs to an almost insignificant degree. 1,3,5-trimethyl-6-(α-methoxyethyl)-benzene (IV) is formed by the reaction of mesityl magnesium bromide with α-monochloroethylmethyl ether (Expt. 9). The product of the second direction of the reaction, 1,3,5-trimethyl-6-(α-chloroethyl)-benzene (V) is formed in an almost insignificant amount (5.3%).

Duryl magnesium bromide reacts similarly to mesityl magnesium bromide, the reaction of which with the same α-monochloroethylmethyl ether leads to the formation of 1,2,4,5-tetramethyl-6-(α-methoxyethyl)-benzene (VI) (Expt. 9). The second product of the reaction, 1,2,4,5-tetramethyl-6-(α-chloroethyl)-benzene (VII), was also obtained in a very small amount (4.7%).


(IV)


(V)

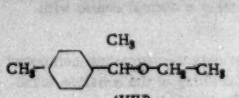

(VI)

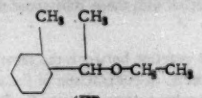

(VII)

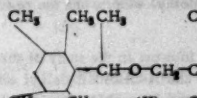
The second representative of the α-chloroethylalkyl ether group, namely, α-monochlorodiethyl ether, differs little in its chemical properties from α-monochloroethylmethyl ether. This difference lies only in its still greater thermal instability as compared to α-monochloroethylmethyl ether. The reaction characteristics of these ethers with organo-magnesium compounds are therefore the same. 1-Methyl-4-(α-ethoxyethyl)-benzene (VIII) is formed as the only product of the reaction of p-tolyl magnesium bromide with α-monochlorodiethyl ether (Expt. 10).

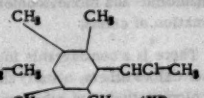
The only product of the reaction of o-tolyl magnesium bromide with α-monochlorodiethyl ether is 1-methyl-2-(α-ethoxyethyl)-benzene (IX) (Expt. 11).

Finally, duryl magnesium bromide, reacting with the same chloroether, forms 1,2,4,5-tetramethyl-6-(α-ethoxyethyl)-benzene(X) as the main reaction product (Expt. 12). The amount of the secondary reaction product, 1,2,4,5-tetramethyl-6-(α-chloroethyl)-benzene (XI) is almost insignificant (3.5%).


(VIII)


(IX)


(X)


(XI)

Returning once more to the question of the reasons for the unusual reaction between orthodisubstituted aryl magnesium halides and chloromethyl ethers, it must be emphasized that the explanation that the reason for the anomalous direction of the reaction is steric in character is upheld by the fact that the reaction between the same organo-magnesium compounds and the chloroethylalkyl ethers is normal in character. If the formation of the benzyl chlorides was a result of secondary processes, then, on the strength of the chemical and thermal instability of the chloroethers, these processes should have taken place to a greater extent with the α-chloroethylalkyl ethers than with the chloromethyl alkyl ethers because the former are less stable chemically and thermally than the latter.

EXPERIMENTAL

The usual conditions for the reaction between the aryl magnesium bromides and the chloromethylalkyl ethers were: A solution of the aryl magnesium bromide in ether (3 volumes) was added slowly, with mechanical stirring and cooling of the reaction flask in ice water, to a solution of the chloromethylalkyl ether in three volumes of absolute ether. This order of addition was used for the orthodisubstituted aryl magnesium bromide because with the reverse, the benzyl chloride which forms then reacts with the residual magnesium, leading to the formation of symmetrical arylethane hydrocarbons. This and the opposite (usual) order of addition can be used with orthomonosubstituted aryl magnesium halides because in both cases only ethers are formed. After the mixing of the reaction components, the mixture was heated for a certain time (usually one hour), and then decomposed with water with cooling. The ether layer was washed in a separatory funnel first with water, then with a 10% sodium bicarbonate solution, and again three times with water. After drying the ether with fused

sodium sulfate, the ether was distilled, the reaction product was redistilled in vacuo, and then analyzed.

1. Reaction of duryl magnesium bromide with monochloromethylethyl ether. Duryl bromide normally only reacts with magnesium in the presence of some low molecular weight alkyl halide, particularly ethyl bromide [2,3], so that the following starting materials were used: 35.5 g (1/6 mole) duryl bromide, 18.2 g (1/6 mole) of ethyl bromide, 10 g of magnesium, and 32 g (1/3 mole) of monochloromethylethyl ether. The reaction was run according to the above conditions. The reaction was run according to the above conditions. The reaction products were vacuum distilled at 12 mm: Fraction I—to 115°; Fraction II from 115-145° —19 g, the residue, 1.5 g. The second fraction was analyzed to determine the amount of 2,3,5,6-tetramethylbenzyl chloride in it (by heating a weighed amount of the product with a saturated alcoholic solution of silver nitrate and then analyzing the silver chloride [4] and ethyl-2,3,5,6-tetramethylbenzyl ether formed).

0.1341 g substance: 0.0759 g AgCl. Found %: Cl 14.0. 0.1128 g substance: 0.0265 g AgI. Found %: OC_2H_5 4.5.

These figures can be used to show that Fraction II contained 72.0% of 2,3,5,6-tetramethylbenzyl chloride and 19.1% of ethyl-2,3,5,6-tetramethylbenzyl ether. On calculating for a pure mixture of the chloride and the ether, these figures corresponded to 79 and 21%.

Because the second fraction crystallized very rapidly after redistillation, the crystals of 2,3,5,6-tetramethylbenzyl chloride were filtered off on a Buchner funnel from the liquid part, and purified by recrystallization from petroleum ether. M.p. 85-86°.

0.1134 g substance: 0.0851 g AgCl. Found %: Cl 18.56. $C_{11}H_{15}Cl$. Calculated %: Cl 19.12.

Upon heating with sodium ethylate, the above chloride was changed to ethyl-2,3,5,6-tetramethylbenzyl ether (not listed in the literature).

B.p. 121-122° (8 mm).

0.1226 g substance: 0.3639 g CO_2; 0.1120 g H_2O. Found %: C 81.00; H 10.22. $C_{13}H_{20}O$. Calculated %: C 81.19; H 10.49.

2. Reaction of pentamethylphenyl magnesium bromide with monochloromethylether. Pentamethylphenyl bromide, like duryl bromide, only reacts with magnesium in the presence of ethyl bromide so that the following were used to run the reaction: 45 g (0.2 mole) pentamethylphenyl bromide, 21.8 g (0.2 mole) ethyl bromide, 12 g magnesium, and 32.2 g (0.4 mole) monochloromethyl ether. The reaction mixture was heated for one hour. The following fractions were obtained on vacuum distillation.

Fraction I, to 120° (7 mm) —11.4 g; Fraction II, 120-155° (7 mm) —19.0 g; residue —2.0 g.

For determination of the amount of pentamethylbenzyl chloride in the second fraction, a weighed amount was heated with a portion of an alcoholic solution of silver nitrate.

0.1244 g substance: 0.0648 g AgCl. Found %: Cl 12.88.

The amount of pentamethylbenzyl chloride in the fraction was 71.4%.

A quantitative determination of the methyl group showed the amount of methylpentamethylbenzyl ether in the fraction:

0.1181 g substance: 0.0358 g AgI. Found %: OCH_3 4.0.

This corresponds to 24.8% of methylpentamethylbenzyl ether in the fraction. By recalculating for a pure mixture of the chloride and the ether, these figures will be 74.2 and 25.8%.

To change the above chloride into the ether, the second fraction was worked up with sodium methylate in a methyl alcohol solution by heating for 15 minutes. The methylpentamethylbenzyl ether obtained had a b.p. 128-130° at 7 mm. M.p. 44° (from petroleum ether). This ether is not listed in the literature.

0.1204 g substance: 0.3575 g CO_2; 0.1114 g H_2O. 0.1289 g substance: 0.1483 g AgI. Found %: C 81.04; H 10.35; OCH_3 15.2. $C_{13}H_{20}O$. Calculated %: C 81.25; H 10.41; OCH_3 16.1.

3. Reaction of mesityl magnesium bromide and monochloromethyl ether. a) The influence of prolonged heating. In order to answer the question of the change of the composition of the product and its quantitative yield upon lengthening the heating time of the reaction mixture, three extra experiments were made under almost

identical conditions. Only the heating time was varied, from 1-5 hours. The reactants (mesityl magnesium bromide and monochloromethyl ether) were taken in 1/7 mole quantities. The main fractions were taken at 95-115° at 6 mm, and were analyzed for the amount of 2,4,6-trimethylbenzyl chloride in them [4]. The weight of the main fractions was from 13.7-14.0 g. The results are listed in Table 1.

This data indicates that when the heating time of the reaction mixture is increased the quantitative yield of the product stays the same, although the 2,4,6-trimethylbenzyl chloride content decreases somewhat.

b) Influence of variation in the ratio of the reactants. In order to answer this question three experiments were made once more. An ether solution of mesityl magnesium bromide prepared from 120 g of mesityl bromide was divided into three equal parts (of 0.2 mole) and each part was then added separately to three different weights of monochloromethyl ether, (12.1, 16.1, and 20.1 g), dissolved in absolute ether. The reaction mixture was then heated for one hour. The main fractions were taken at 95-115° at 6 mm, and analyzed for the amount of 2,4,6-trimethyl-benzyl chloride in them [4]. The weight of the main fraction in the first experiment was 16.2 g, in the second 18.0 g, and in the third 20.1 g. The amount of 2,4,6-trimethylbenzyl chloride in the main fractions is listed in Table 2.

The results of these experiments indicate that when the amount of monochloromethyl ether is increased, the yield of the product, as well as the amount of 2,4,6-trimethylbenzyl chloride in it, is increased.

c) Determination of the comparative stability of orthosubstituted methylbenzyl ethers to the action of monochlorodimethyl ether. Methyl-2-methylbenzyl and methyl-2,4,6-trimethylbenzyl ethers in 10 g quantities dissolved in ether (3 volumes) were used in the determination of the comparative stability of ortho mono- and disubstituted methyl benzyl ethers to the action of monochlorodimethyl ether. These ethers were heated for 3 hours with a quantity (7 g) of monochlorodimethyl ether. Water was then added to the reaction mixture and the ether layer was washed with a sodium carbonate solution and again with water. After drying the ether solution, the solvent was distilled and the residue was vacuum distilled (wherein the boiling point of the ether almost did not change) and analyzed for chloride.

On heating methyl-2-methylbenzyl ether with the above chloroether, 0.24% of 2-methylbenzyl chloride was formed.

0.5013 g substance: 0.0013 g AgCl. Found %: Cl 0.06.

On heating methyl-2,4,6-trimethylbenzyl ether with the same chloroether, 3.5% of 2,4,6-trimethylbenzyl chloride was formed.

0.5247 g substance: 0.0156 g AgCl. Found %: Cl 0.74.

Similar results are obtained on heating the above substance in the presence of $MgCl_2$ (3 g).

4. Reaction of mesityl magnesium bromide with monobromodimethyl ether. The method of Hamonet [5], employing the reaction of gaseous HBr with monochlorodimethyl ether, was used to prepare monobromodimethyl ether.

$$CH_2Cl{-}O{-}CH_3 + HBr \longrightarrow CH_2Br{-}O{-}CH_3 + HCl.$$

HBr was passed in until saturation into the chloroether, and the monobromodimethyl ether which formed was redistilled from the flask through a dephlegmator. B.p. 86-87°.

40 g (0.2 mole) of mesityl bromide, 6 g of magnesium, and 25 g (0.2 mole) of monobromodimethyl ether were used for the experiment. An ether solution of the organo-magnesium compound was added to the monobromodimethyl ether. The reaction mixture was heated for one hour. Fraction 1, to 87° (6 mm); Fraction 2, 87-140° (6 mm); —22 g; residue 1.5 g.

The subsequent analysis of the second fraction was done in the previously given manner.

0.1171 g substance: 0.0084 g AgBr. Found %: Br 3.05. 0.1311 g substance: 0.1581 g AgI. Found %: OCH_3 15.9.

Therefore the second fraction contains 8.3% of 2,4,6-trimethylbenzyl bromide and 84.2% of methyl-2,4,6-trimethylbenzyl ether. On recalculation for a pure mixture, these figures equal 9 and 91%.

After purification of the second fraction by heating with sodium methylate, followed by rectification,

methyl-2,4,6-trimethylbenzyl ether with b.p. 95-97° (7 mm) was obtained. In the literature [7], b.p. 109-110° at 15 mm is given for this compound. Yield 13.5 g (40%).

0.1215 g substance: 0.1601 g AgI. Found %: OCH_3 17.4. $C_{11}H_{16}O$. Calculated %: OCH_3 18.9.

5. Reaction of mesityl magnesium bromide with monoiodomethyl ether. For the preparation of monoiodomethyl ether, Henry [6] recommends that a mixture of formalin and methyl alcohol be saturated with gaseous HI. As this procedure was not very convenient technically, another procedure based upon the reaction of KI with monochloromethyl ether was used.

Well-dried and pulverized potassium iodide was placed into a flask provided with a reflux condenser. While the flask was cooled in an ice-salt mixture, the monochlorodimethyl ether was slowly added to it. To complete the reaction, the reaction flask was heated on the water bath for one hour. Because monoiodomethyl ether is so thermally unstable and decomposes completely into methyl iodide and polyoxymethylene for purification it was vacuum distilled. B.p. 39° at 20 mm.

40 g (0.2 mole) of mesityl bromide, 6 g of magnesium, and 34.4 g (0.2 mole) of monoiodomethyl ether were used for the reaction of mesityl magnesium bromide and monoiodomethyl ether. The ether solution of mesityl magnesium bromide was separated from the residual magnesium and added to the monoiodomethyl ether. The reaction mixture was heated for a period of one hour. Fraction I, to 92° (9 mm), Fraction II, 92-155° (9 mm) —24.0 g; residue —1.5 g.

The second fraction contained the iodide and the ether, whose quantities were determined by the earlier-given methods.

0.1238 g substance: 0.0021 g AgI. Found %: I 0.92. 0.1361 g substance: 0.1711 g AgI. Found %: OCH_3 16.6.

These figures indicate the following quantitative composition for the above substances in Fraction II: 2,4,6-trimethylbenzyl iodide 2.3% and methyl-2,4,6-trimethylbenzyl ether 87.8%. On calculating for a pure mixture, these figures are equal to 2.6 and 97.4%. After purification of Fraction II with sodium methylate, followed by rectification, methyl-2,4,6-trimethylbenzyl ether, b.p. 92-93° (5 mm) was obtained.

0.1197 g substance: 0.1632 g AgI. Found %: OCH_3 18.0. $C_{11}H_{16}O$. Calculated %: OCH_3 18.9.

6. Reaction of p-tolyl magnesium bromide with α-chloroethylmethyl ether. 42.8 g (0.25 mole) of p-bromotoluene, 7 g of magnesium, and 23.6 g (0.25 mole) of α-monochloroethylmethyl ether were used for the experiment. The conditions given above were used for the reaction. For this group of experiments only one order of addition of the reaction components were used: the ether solution of the organo-magnesium compound decanted from the residual magnesium was added to an ether solution of the chloroether. After mixing the reaction components, the reaction mixture was heated for one hour and then decomposed with water, with cooling, and, if the ether layer remained cloudy, with 10% acetic acid. The mixture was transferred to a separatory funnel, the lower aqueous layer was separated, the ether layer was washed first with a 5% solution of sodium bicarbonate, and then three times with water.

Since benzyl chlorides, and especially those containing a chlorine on a secondary carbon atom, are prone to hydrolysis, the possibility of this occurring was tested by determining the hydroxyl groups in the reaction product by Chugaev's method. The above method of washing the ether layer was not used until it was established that no appreciable hydrolysis occurred.

After the ether solution was dried with fused sodium sulfate, the ether was distilled, the reaction product fractionated and then analyzed. Fraction I, to 70° (9 mm); Fraction II, 70-100° (9 mm) —18.0 g; Fraction III, 100-150° (9 mm) —4.0 g; residue —1.5 g.

Because no silver chloride could be obtained on treating Fraction II with alcoholic silver nitrate, showing that no noticeable amount of 1-methyl-4-(α-chloroethyhyl)-benzene was present, Fraction II was refractionated, resulting in the separation of 1-methyl-4-(α-methoxyethyl)-benzene, b.p. 72-73° at 8 mm. Yield 14 g (38%). A final purification of this ether by heating with sodium methylate in a methyl alcohol solution did not change the boiling point. This ether is not listed in the literature.
n_D^{20} 1.4930; d_4^{20} 0.9300; MR_D 46.94; calculated 46.42.

0.1019 g substance: 0.2978 g CO_2; 0.0858 g H_2O. 0.1490 g substance: 0.2110 g AgI. Found %: C 79.75; H 9.42; OCH_3 18.71. $C_{10}H_{14}O$. Calculated %: C 79.95; H 9.39; OCH_3 20.65.

Fraction III (100-150° at 9 mm) was dissolved in ethyl alcohol and cooled. The crystals of di-p-tolyl which separated melted at 121° after purification by twofold recrystallization. The literature [8] gives m.p. 120° for di-p-tolyl.

0.1299 g substance: 0.4385 g CO_2; 0.0907 g H_2O. Found %: C 92.11; H 7.81. $C_{14}H_{14}$. Calculated %: C 92.26; H 7.74.

7. Reaction of o-tolyl magnesium bromide with α-monochloroethylmethyl ether. 34.2 g (0.2 mole) o-bromotoluene, 6 g of magnesium, and 18.9 g (0.2 mole) of α-monochloroethylmethyl ether were used for the reaction. The usual reaction conditions given above were used. Fractionation of the product obtained gave the following results: Fraction I, to 82° (20 mm); Fraction II, 82-95° (20 mm) –14.6 g; residue –1.5 g.

For the determination of the amount of 1-methyl-2-(α-chloroethyl) benzene in the second fraction, a weighed amount was heated with an alcoholic silver nitrate solution.

0.4202 g substance: 0.0043 g AgCl. Found %: Cl 0.25. The amount of 1-methyl-2-(α-chloroethyl)-benzene in the substance is equal to 1.1%.

The remainder of Fraction II was then heated with sodium methylate dissolved in methyl alcohol in order to convert the 1-methyl-2-(α-chloroethyl)-benzene present to 1-methyl-2-(α-methoxyethyl)-benzene. After a final fractionation of the purified substance, 1-methyl-2-(α-methoxyethyl)-benzene, b.p. 90-91° at 25 mm, was isolated. Yield 12 g (40%). This ether is not listed in the literature.

n_D^{20} 1.4989; d_4^{20} 0.9433; MR_D 46.71; calculated 46.42.

0.1338 g substance: 0.3909 g CO_2; 0.1124 g H_2O. 0.1634 g substance: 0.2398 g AgI. Found %: C 79.72; H 9.40; OCH_3 19.38. $C_{10}H_{14}O$. Calculated %: C 79.95; H 9.39; OCH_3 20.65.

8. Reaction of α-naphthyl magnesium bromide with α-monochloroethylmethyl ether. Starting materials: 69 g (1/3 mole) of α-bromonaphthalene, 9 g magnesium, and 31.5 g (1/3 mole) of α-monochloroethylmethyl ether.

The usual reaction conditions were used. Fraction I, to 125° (13 mm); Fraction II, 125-145° (13 mm) –45.0 g; residue –3.0 g.

Silver chloride did not separate when a weighed amount of Fraction II was heated with alcoholic silver nitrate, which indicated that 1-(α-chloroethyl)-naphthalene was not present in the reaction product. On a further fractionation of the second fraction, 1-(α-methoxyethyl)-naphthalene, b.p. 109-110° at 3 mm, was isolated. Yield 31 g (50%). A final purification of the ether by heating it for 10 minutes with sodium methylate in methyl alcohol solution did not change the boiling point. This ether is not listed in the literature.

n_D^{20} 1.5931; d_4^{20} 1.0490; MR_D 60.61; calculated 57.14 (ME 3.47).

0.2190 g substance: 0.6744 g CO_2; 0.1458 g H_2O. 0.5308 g substance: 0.6558 g AgI. Found %: C 84.03; H 7.45; OCH_3 16.33. $C_{13}H_{14}O$. Calculated %: C 83.83; H 7.58; OCH_3 16.66.

9. Reaction of mesityl magnesium bromide with α-monochloroethylmethyl ether. 50.0 g (0.25 mole) mesityl bromide, 7 g of magnesium, and 23.6 g (0.25 mole) of α-monochloroethylmethyl ether were used. The usual reaction conditions were used.

Fraction I, to 80° (6 mm); Fraction II, 83-120° (6 mm); 20.2 g; residue –2.0 g.

For determination of the amount of 1,3,5-trimethyl-6-(α-chloroethyl)-benzene in the second fraction, a weighed amount was heated, as usual, for 15 minutes with an alcoholic silver nitrate solution.

0.4122 g substance: 0.0176 g AgCl. Found %: Cl 1.05. The amount of 1,3,5-trimethyl-6-(α-chloroethyl)-benzene in the reaction product corresponds to 5.3 %.

In order to transform the above chloride in the product in the remainder of Fraction II to 1,3,5-trimethyl-6-(α-methoxyethyl)-benzene, it was heated with sodium methylate in methyl alcohol. The 1,3,5-trimethyl-6-(α-methoxyethyl)-benzene which was isolated from the final fractionation of the product purified with sodium methylate had b.p. 92-94° at 7 mm.

n_D^{20} 1.5052; d_4^{20} 0.9451; MR_D 55.96; calculated 55.66.

0.1574 g substance: 0.4642 g CO_2; 0.1418 g H_2O. 0.2898 g substance: 0.3468 g AgI. Found %: C 80.43; H 10.08; OCH_3 15.80. $C_{22}H_{30}O$. Calculated %: C 80.84; H 10.17; OCH_3 17.30.

This ether is not listed in the literature.

10. Reaction of duryl magnesium bromide with α-monochloroethylmethyl ether. Starting materials: 35.5 g (1/6 mole) duryl bromide, 18.1 g (1/6 mole) of ethyl bromide, 11 g of magnesium, and 31.5 g (1/3 mole) of α-monochloroethylmethyl ether.

The usual reaction conditions were used for the reaction studied. Fraction I, to 97° (7 mm); Fraction II, 97-130°, −15.0 g; residue −2.0 g.

The second fraction contains an insignificant amount of the second reaction product, 1,2,4,5-tetramethyl-6-(α-chloroethyl)-benzene.

0.3843 g substance: 0.01351 g AgCl. Found %: Cl 0.87.

The amount of the above chloride in the reaction product corresponds to 4.7%.

In order to make the whole reaction product more homogeneous, Fraction II was heated with sodium methylate in methyl alcohol. The 1,2,4,5-tetramethyl-6-(α-methoxyethyl)-benzene isolated after a final recrystallization from alcohol had m.p. 109-110°. There is no report of this ether in the chemical literature.

0.1102 g substance: 0.3272 g CO_2; 0.1032 g H_2O. 0.1524 g substance: 0.1642 g AgI. Found %: C 80.97; H 10.47; OCH_3 14.23. $C_{13}H_{20}O$. Calculated %: C 81.19; H 10.48; OCH_3 16.91.

11. Reaction of p-tolyl magnesium bromide with α-monochlorodiethyl ether. 43 g (0.25 mole) of p-bromotoluene, 7 g of magnesium, and 27.1 g (0.25 mole) of α-monochlorodiethyl ether were used for the reaction.

Fractionation of the mixture of substances obtained gave the following results: Fraction I, to 75° (12 mm); Fraction II, 75-110°. (12 mm) −21.5 g; residue 3.5 g.

Heating a weighed amount of Fraction II with an alcoholic silver nitrate solution did not produce any silver chloride, showing the absence of 1-methyl-4-(α-chloroethyl)-benzene in the above fraction. On refractionating Fraction II, 1-methyl-4-(α-ethoxyethyl)-benzene, b.p. 82-83° at 12 mm, was isolated. Yield 18 g (44%). A final purification of the product with sodium ethylate in ethyl alcohol did not change the boiling point.

n_D^{20} 1.4841; d_4^{20} 0.9122; MR_D 51.52; calculated 51.04.

0.1091 g substance: 0.3209 g CO_2; 0.0965 g H_2O. 0.1077 g substance: 0.1415 g AgI. Found %: C 80.27; H 9.90; OC_2H_5 25.2. $C_{11}H_{16}O$. Calculated %: C 80.44; H 9.82; OC_2H_5 27.4.

This ether is not listed in the literature. The residue after the distillation of the main product (3.5 g) crystallized in the flask. Crystals of di-p-tolyl, m.p. 121° were obtained after two recrystallizations from ethyl alcohol. The mixed melting point with synthetic di-n-tolyl was 121°, no depression in the melting point.

0.1155 g substance: 0.3902 g CO_2; 0.0803 g H_2O. Found %: C 92.20; H 7.78. $C_{14}H_{14}$. Calculated %: C 92.26; H 7.74.

12. Reaction of o-tolyl magnesium bromide with α-monochlorodiethyl ether. 43 g (0.25 mole) of o-bromotoluene, 7 g of magnesium, and 27.1 g (0.25 mole) of α-monochlorodiethyl ether were used for the reactions. The reaction conditions were those given earlier. Fraction I, to 77° (12 mm); Fraction II, 77-110° (12 mm) −19.5 g; residue −1.5 g. The amount of the chloride in Fraction II was determined by heating a weighed amount of this fraction with an alcoholic silver nitration solution.

0.1521 g substance: 0.0014 g AgCl. Found %: Cl 0.22. The amount of 1-methyl-2-(α-chloroethyl)-benzene was equal to 1.0%. After heating Fraction II with an ethyl alcohol solution of sodium ethylate, followed by a fractionation, 1-methyl-2-(α-ethoxyethyl)-benzene, b.p. 84-85° at 12 mm, was isolated.

n_D^{20} 1.4863; d_4^{20} 0.9263; MR_D 50.98; calculated 51.04.

0.1173 g substance: 0.3448 g CO_2; 0.1034 g H_2O. 0.1015 g substance: 0.1294 g AgI. Found %: C 80.22; H 9.86; OC_2H_5 24.5. $C_{11}H_{16}O$. Calculated %: C 80.44; H 9.82; OC_2H_5 27.4.

This ether is not listed in the chemical literature.

13. Reaction of duryl magnesium bromide with α-monochlorodiethyl ether. Starting materials: 35.5 g (1/6 mole) duryl bromide, 18 g (1/6 mole) ethyl bromide, 11 g of magnesium, and 36.2 g (1/3 mole) of α-monochlorodiethyl ether. Fraction I, to 112° (8 mm); Fraction II, 112-127° (8 mm) —16.0 g; residue —1.5 g.

As in the previous experiments, a weighed amount of Fraction II was warmed with alcoholic silver nitrate, to determine the amount of 1,2,4,5-tetramethyl-6-(α-chloroethyl)-benzene.

0.4005 g substance: 0.0128 g AgCl. Found %: Cl 0.79.

Thus the amount of the chloride in Fraction II is equal to 3.5%.

Fraction II was purified with sodium ethylate, followed by distillation and subsequent recrystallization from alcohol to give 1,2,4,5-tetramethyl-6-(α-ethoxyethyl)-benzene, m.p. 52-53° Yield 13.0 g (38%). This ether is not listed in the literature.

0.1139 g substance: 0.3393 g CO_2; 0.1101 g H_2O. 0.1081 g substance: 0.1161 g AgI. Found %: C 81.29; H 10.82; OC_2H_5 20.6. $C_{14}H_{22}O$. Calculated %: C 81.50; H 10.75; OC_2H_5 21.8.

SUMMARY

1. The unusual reaction between aryl magnesium halides and chloromethylalkyl ethers, in which orthodisubstituted aryl magnesium halides, in contrast to the orthomonosubstituted and unsubstituted, react with the above ethers to form the corresponding benzyl chlorides and not the normal products, the ethers, has been confirmed by new experimental material.

2. An experimentally upheld opinion as to the reason for this unusual reaction is given.

3. Monobromo- and monoiodomethyl ethers which are more active in comparison to monochloromethyl ether react normally, in contrast to the latter, with the orthodisubstituted aryl magnesium halides to form ethers, $R{-}CH_2{-}O{-}CH_3$. The benzyl bromides and iodides are formed only in almost insignificant amounts in these reactions.

4. α-Monochloroethylalkyl ethers, because of the greater activity of the chlorine atom as compared to the monochloroalkyl ethers, react with the aryl magnesium bromides to form normal reaction products, that is ethers of the type $R{-}CH(CH_3){-}O{-}R$. The second reaction, namely that forming the chlorides, $R{-}CHCl{-}CH_3$, only takes place with reactions with orthodisubstituted aryl magnesium halides and then only to a very insignificant extent.

5. In the process of this work, eleven substances, as yet unreported in the chemical literature, were synthesized and reported.

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THE PHENYLAMIDATION OF CARBOXYLIC ACIDS

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It was found earlier that amides were formed in good yields by the action of sulfonamides on the carboxylic acids [1], and that good yields of dialkyl amides were formed by the action of asymmetrical dialkyl sulfonamides on the carboxylic acids [2].

It was of considerable interest to see if carboxylic acids would be amidated with symmetrically substituted sulfonamides. The easily available sym. diphenylsulfonamide [3] and several aliphatic, aromatic, and heterocyclic acids were used as subjects for the experiments. It was found that the reaction proceeded very readily according to the following general reaction scheme:

$$RCOOH + C_6H_5NHSO_2NHC_6H_5 \longrightarrow RCONHC_6H_5 + C_6H_5NHSO_2OH.$$

Up to now one exception has been found, namely, the reaction of formic acid, which proceeds according to the following scheme:

$$HCOOH + 2C_6H_5NHSO_2NHC_6H_5 \longrightarrow HC(=NC_6H_5)(NHC_6H_5) + 2C_6H_5NHSO_2OH,$$

i.e., the formation of diphenylformamidine (with a yield of 86.7%) and not formanilide.

The yields of the phenylamides (acylanilides) are very good (see the Experimental section), in most cases over 90% of theory, and in some cases practically quantitative.

The direct phenylamidation of carboxylic acids can undoubtedly be used for the isolation and identification of the carboxylic acids because, as we know, the acylanilides are difficultly soluble in water and crystallize well. Only a few hundreds of a gram of the acid and a very short time are needed for the preparation of the necessary amount of the acylanilide for identification. The possibility that this reaction will be used industrially can not be excluded especially if good methods for the preparation of nuclear substituted diphenylsulfonamides can be found.

Name of acid	Yield of phenylamide % of theory	Recrystallization solvent for phenylamides	Melting points	
			Found	Literature values
Acetic	77.7	Water	114-115°	115°
Probionic	87.2	Alcohol + water	102-103	103-104
Isovaleric	79.1	Alcohol + water	103-105	109-111
Palmitic	89.7	Alcohol	83-84	87.5-90
Stearic	94.7	Alcohol	93-94	93.6
Phenylacetic	97.1	Alcohol + water	116-117	116-117
Benzoic	90.3	Alcohol	160-161	160-161
o-Chlorobenzoic	95.1	Alcohol	115-116	115
m-Nitrobenzoic	99.1	Alcohol	152-153	153-154
p-Nitrobenzoic	100.0	Alcohol	211-212	204
Nicotinic	80.8	Water (with $2H_2O$)	83-85	85 [5]

EXPERIMENTAL

A mixture of 0.01 mole of the carboxylic acid, 0.01 mole of symmetrical diphenylsulfonamide (2.24 g), and 5 ml of dry pyridine were heated in a 50-ml round-bottomed flask with a side arm for four hours on an oil bath heated to 115-120°. The pyridine was vacuum distilled to dryness on a boiling water bath, and the residue was worked up with 25 ml of 1N sodium hydroxide. The residue, in certain cases, had to be rubbed with a glass rod for some time in order to crystallize it. The phenylamide was then filtered, washed 4 times with (3 ml) water, and dried. In most cases almost colorless preparations were obtained, which melted only a few degrees below the pure substances. Completely pure acylanilides were obtained after one recrystallization.

The table contains the yield and melting point data of all of the phenylamides obtained by the direct phenylamidation of the carboxylic acids.

The yields of the acylanilides, noticeably soluble in water could probably be increased by extracting the aqueous filtrates and washings ether, or some other suitable solvent, after removal of the acylanilides.

The diphenylformamidine was prepared and isolated in a manner similar to that used with the phenylamides, but for 0.01 mole or dry formic acid (0.46 g), 0.02 mole of diphenylsulfonamide (4.96 g) was used. The yield was 1.7 g, i.e., 86.7% of theory. The preparation melted at 136-137° after recrystallization from petroleum ether; according to the literature, diphenylformamidine melts at 135-136°, 138-139° [4].

SUMMARY

A method for the preparation of acylanilides by reacting the corresponding acids directly with diphenylsulfonamide was found.

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TRIMESINIC TRIANILIDE

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Curtius [1] obtained trimesinic trianilide in crystal form (from acetic acid), m.p. 118-120° (decomp.), by the prolonged heating of trimesinic triazide with aniline.

A trimesinic trianilide which darkened at 317° and melted at 320-321° when heated in a capillary was obtained by the action of diphenylsulfonamide [2] on trimesinic acid.

Usually the anilides of the lower melting carboxylic acids melt considerably higher than the free acids, and the anilides of the higher melting carboxylic acids melt either somewhat higher or lower than the free acids, not more than 40-50° [3]. The melting points of the amides and anilides of the higher melting carboxylic acids also do not differ by more than 40-50° [3]. The melting point of trimesinic acid is 350°, that of its amide 365° [3]; therefore it seemed very surprising that the anilide of trimesinic acid would melt at 118-120°. Apparently there is some error in the work of Curtius. In order to finally clear up this misunderstanding, the trimesinic trianilide, obtained by direct phenylamidation of trimesinic acid, was analyzed for its nitrogen, carbon, and hydrogen content. The quantities of nitrogen, carbon, and hydrogen corresponded to those for the trianilide. Therefore the melting point for trimesinic anilide should be corrected from 118-120° to 320-321°.

EXPERIMENTAL

A mixture of 0.05 mole of trimesinic acid (1.05 g), 0.015 mole of diphenylsulfonamide (3.72 g), and 7.5 ml of dry pyridine was heated for 3 hours on an oil bath heated to 115°. The pyridine was vacuum distilled, 25 ml of 1.0 N sodium hydroxide was added to the residue, and the pasty residue rubbed with a rod until it completely crystallized, which occurred after 4-5 minutes. The finely crystalline residue was filtered, carefully washed with water, and dried. The yield of trimesinic trianilide was 2.0 g, that is, 91% of theory. The substance was purified by recrystallizing it from a large amount of boiling alcohol (600 ml per g) or from boiling acetic acid (40 ml of acetic acid for 1 g). Yield, 0.80 g; coarse needles.

Trimesinic trianilide formed a finely crystalline colorless powder (from alcohol) or colorless shiny needles (from acetic acid). Trimesinic trianilide was difficultly soluble in all the common solvents. It darkened at 317° and melted at 320-321° (Berle-Coleman block, narrow range thermometer).

Found %: C 74.00; H 4.78; N 9.71. $C_{27}H_{21}O_3N_3$. Calculated %: C 74.42; H 4.86; N 9.65.

The authors are very grateful to N. A. Ilushin of the Organic Chemistry Institute of the Academy of Sciences of the USSR for the analysis of the compound.

SUMMARY

Trimesinic trianilide was produced by the direct phenylamidation of trimesinic acid, and was found to melt at 320-321°, and not at 118° as held by Curtius.

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* See Consultants Bureau translation, p. 1653.

HYDROXYMETHYLENE-(PHENYL) ACETIC ACID AND ITS DERIVATIVES

I. T. Strukov

In the present research, several derivatives of hydroxymethylene-(phenyl) acetic acid were studied in order to become acquainted with the physical and chemical properties of this series of organic compounds.

In Communication II [1], it was shown that hydroxymethylene-(phenyl) acetic acid could be prepared from diethoxymethyl-(phenyl) acetic acid by treating it with concentrated hydrochloric acid at 0°. In contrast to the method given in the literature [2], diethoxymethyl-(phenyl) acetic acid was prepared directly from formyl-(phenyl) acetic ester by heating it with an alcoholic solution of hydrochloric acid, followed by the saponification of the ester.

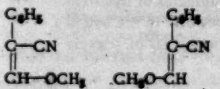
The unusual change in hydroxymethylene-(phenyl) acetic acid when dissolved in pyridine, its condensation with cysteine hydrochloride, as well as its unusually facile decarboxylation reaction, are of great theoretical interest.

Hydroxymethylene-(phenyl) acetic acid, its amide, and nitrile exist, mainly, in the hydroxymethylene form, as shown by the color reaction with ferric chloride and by the absence of a reducing group when added to ammoniacal silver. However, the derivatives, are not only hydroxymethylene forms, but also the aldehydic forms of these compounds. For example, when diethoxymethyl-(phenyl) acetic acid (I) is reacted with thionyl chloride in chloroform, a molecule of ethanol is split off and ethoxymethylene-(phenyl) acetic acid (II) is formed.

(I) (II)

Substance (I) is derived from the aldehyde and (II) is the hydroxymethylene form.

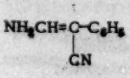
Methoxymethylene-(phenyl)-acetetonitrile is rather easily formed by the action of dimethyl sulfate on the sodium salt of hydroxymethylene-(phenyl)-acetonitrile [3]. Two forms of this compound are obtained, apparently the cis and trans forms. The cis form is a liquid (III), the trans form — a solid substance, m.p. 65-67° (IV).



(III) (IV)

Both forms are easily saponified by alcoholic alkalies and form hydroxymethylene-(phenyl)-acetonitrile. Benzyl cyanide is obtained at the same time.

Hydroxymethylene-(phenyl)-acetonitrile must be looked upon as an acid, and methoxymethylene-(phenyl)-acetonitrile as the ester of this acid. In fact, aminomethylene-(phenyl)-acetonitrile (V) is formed when the latter is treated with alcoholic ammonia.



(V)

Methoxymethylene-(phenyl)-acetonitrile does not give an iminoether. This is the latest differentiation of this compound from the nitriles. Although hydroxymethylene-(phenyl)-acetonitrile is not known in the aldehydic form, it is, however, apparently able to exist at certain times in the tautomeric aldehydic form, so that when it is heated with alcoholic hydrogen chloride, the acetal, diethoxymethoxy-(phenyl)-acetonitrile is formed, although not in good yield.

Ethyl aminomethylene-(phenyl)-acetate is obtained, instead of aminoethylene-(phenyl)-acetamide, by the action of alcoholic ammonia on ethyl methoxymethylene-(phenyl)-acetate (preparation [1]). Apparently in the above case, the methoxymethylene group behaves as an ester, being more labile than the usual ester group. Ethyl aminomethylene-(phenyl)-acetate has a peculiarity of its own: it forms diethyl iminobis-[methylene-(phenyl)-acetate] when treated with ethereal hydrogen chloride. Since similar transformations are unknown

for usual amides, a very probable assumption can be made that the reaction occurs by means of the tautomeric form of aminomethylene-(phenyl)acetic ester (VI), the iminomethyl-(phenyl)-acetic ester (VII).

(VI) (VII)

Diethyl imino-(bis)-[methylene-(phenyl)-acetate] (VIII) was obtained in two forms, m.p. 152-154° (platelets) and m.p. 122-124° (long needles). There is the possibility of the change of the position of the double bonds in this compound

(VIII)

and there is no basis to consider them as really being cis and trans forms. In fact, if the possibility of the change of the position of the double bonds is excluded and considered to be a case of cis-trans isomerism, then, it is very hard to picture the formation of compound (VIII) from the aminomethylene-(phenyl) acetic ester (VI). Iminomethyl-(phenyl) acetic ester is an acid aldimine by virtue of the easy splitting of the imino group by the action of hydrogen chloride. Diethoxymethyl-(phenyl) acetic ester does not react with ammonia. For this reason diethoxymethyl-(phenyl) acetamide is obtained from diethoxymethyl-(phenyl) acetic acid. The anhydride of this acid is obtained by the action of thionyl chloride in chloroform in the presence of pyridine. Upon processing the anhydride in chloroform solution with aqueous ammonia, diethoxymethyl-(phenyl) acetamide (IX) is obtained in good yield, and on dissolving it in concentrated hydrochloric acid, the unstable hydrochloride of hydroxymethylene-(phenyl)-acetamide, and subsequently, the amide can be isolated.

(IX) (X)

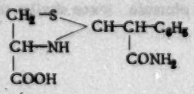
According to its reaction with ferric chloride solution and the absence of reducing power, compound (X) has the hydroxymethylene form. Therefore, in the process of splitting the acetal, the aldehyde group rapidly isomerizes to the hydroxymethylene group. By condensing compound (X) with cysteine hydrochloride, α-(4-carboxythiazolidyl-2)-phenylacetamide (XI) is formed, which shows the easy transformation of the hydroxymethylene-(phenyl)-acetamide into the aldehyde form. The many reaction possibilities of hydroxymethylene-(phenyl) acetamide, due to the reactivity of the hydrogens on the amide group and to the hydroxy group of the hydroxymethylene, is of great interest as a means for the preparation of a new class of organic compounds.

According to their properties, hydroxymethylene-(phenyl) acetic acid, its amide, and its nitrile closely resemble the organic acids and their derivatives, but differ in possessing new capabilities for chemical transformation.

EXPERIMENTAL

Ethoxymethylene-(phenyl) acetic acid. 2 g of freshly distilled thionyl chloride in 5 ml of absolute chloroform was added to 1 g of diethoxymethyl-(phenyl) acetic acid dissolved in 5 ml of absolute chloroform and the mixture left for 18 hours at 20-25°. The chloroform and excess of thionyl chloride were removed by blowing them out with air in a vacuum. The residual oil was dissolved in 10 ml of chloroform and the solution treated with 10 ml of a 5% sodium bicarbonate solution. The water layer was separated, treated with activated charcoal, filtered, and carefully acidified at 0° with dilute hydrochloric acid. A crystalline precipitate (prisms) separated. It was recrystallized from benzene (1:4) to which pentane was added to cloudiness. M.p. 134-135°.

Ethoxymethylene-(phenyl) acetic acid was very soluble in alcohol, ether, acetone, ethyl acetate, and benzene; it was insoluble in water, gasoline, and pentane. The acid decarboxylated at 160°



(XI)

4.921 mg substance: 7.56 ml 0.05 N $Na_2S_2O_3$. Found %: OC_2H_5 23.06. $C_{11}H_{13}O_2$. Calculated %: OC_2H_5 23.96.

Ethoxymethylene-(phenyl)-acetonitrile. 1.6 g of sodium, followed by 8 g of hydroxymethylene-(phenyl)-acetonitrile, was added to 70 ml of absolute ethyl alcohol, whereupon a voluminous light yellow precipitate of the sodium salt formed. 14 g of ethyl iodide was added to the flask and it was heated to reflux for 20 hours, protected by a calcium chloride tube. At the end of the reaction, the solution was filtered from the precipitated sodium salt of hydroxymethylene-(phenyl)-acetonitrile, the alcohol was distilled, and the residue was dissolved in 100 ml of ether. The ether solution was washed with water and dried with sodium sulfate. After removal of the ether, the residual oil was fractionated in vacuum, and a fraction with b.p. 146-148° at 5-6 mm was collected. Weight 2.0 g, a colorless oil.

15.291 mg substance: 8.65 ml 0.01 N H_2SO_4. 15.063 mg substance: 8.50 ml 0.01 N H_2SO_4. Found %: N 7.92, 7.90. $C_{11}H_{11}ON$. Calculated %: N 8.09.

A silver salt, rapidly darkening in the light, was formed by the action of a silver nitrate solution on an aqueous solution of the sodium salt of hydroxymethylene-(phenyl)-acetonitrile.

8 g of the silver salt of hydroxymethylene-(phenyl)-acetonitrile was stirred for 6 hours, at 15° with 10 g of ethyl iodide in 100 ml of water. The reaction mixture was extracted with ether, the ether solution was filtered and dried with sodium sulfate, and the residue distilled in vacuum. 2 g of a colorless oil, b.p. 145-148° at 5-6 mm, was obtained.

Methoxymethylene-(phenyl)-acetonitrile, its cis and trans forms. 74 g of a 42% potassium hydroxide solution was added slowly to 74 g of hydroxymethylene-(phenyl)-acetonitrile in 400 ml of water in a 1-liter round-bottomed flask equipped with a stirrer and immersed in an ice-water bath. [illegible] g of dimethyl sulfate was then added to the solution of the potassium salt of hydroxymethylene-(phenyl)-acetonitrile and the mixture stirred for 15 hours at 0°. A thick, lumpy mass separated. It was separated from the aqueous solution, dissolved in 400 ml of ether, and washed with a 40% potassium hydroxide solution. The ether solution was dried with sodium sulfate, the ether distilled, and the residue vacuum distilled. B.p. 142-145° at 3-4 mm.

Trans-methoxymethylene-(phenyl)-acetonitrile crystallized in the form of long platelets when the distillate was dissolved in 70 ml of warm ether and cooled to −10°. The substance was filtered, washed with cold ether, and recrystallized from ether. M.p. 65-67°. Readily soluble in alcohol, ether, benzene, and poorly in gasoline.

6.260 mg substance: 3.93 ml 0.01 N H_2SO_4. Found %: N 8.79. $C_{10}H_9ON$. Calculated %: N 8.8.

On concentrating the mother liquor to 35-40 ml and cooling it to −10°, a small amount more of crystals, m.p. 65-67°, was obtained. (In all cases the filtration was made on a funnel cooled with ice and salt). The ether was distilled from the second mother liquor and the residual oil cooled to −10°. The crystals which formed were filtered and recrystallized from a mixture of toluene and pentane. M.p. 65-67°.

A total of 26 g of trans-methoxymethylene-(phenyl)-acetonitrile was obtained.

The residual oil was refractionated in vacuum at 3 mm: Fraction I, 120-127°, ~4 g; Fraction II, 127-128°, ~19 g (oil); Fraction III, 128-130°, ~0.5 g.

Fraction II contained cis-methoxymethylene-(phenyl)-acetonitrile. It did not crystallize even after long standing.

7.515 mg substance: 0.5714 mg N_2 (19.5°, 741.5 m). Found %: N 8.65. $C_{10}H_9ON$. Calculated %: N 8.8.

By the saponification of 1 g each of the cis- and trans-methoxymethylene-(phenyl)-acetonitrile with 10 ml of methanol and 3.3 ml of 2.0 N KOH for 48 hours at 15°, with subsequent processing, 0.4 and 0.45 g respectively of hydroxymethylene-(phenyl)-acetonitrile, m.p. 156-158°, were obtained. Thus both forms gave the identical substance.

Benzyl cyanide was detected in the liquors.

An attempt to prepare methoxymethylene-(phenyl)-acetiminoether hydrochloride from methoxymethylene-(phenyl)-acetonitrile by Pinner's method was unsuccessful. The unchanged starting material was recovered.

Diethoxymethyl-(phenyl)-acetonitrile. 23.2 g of hydroxymethylene-(phenyl)-acetonitrile was added to a solution of 1.7 g (preweighed) dry hydrogen chloride in 150 ml of absolute ethanol and the mixture heated to reflux, protected by a calcium chloride tube, for 13 hours on a water bath. Upon cooling, 2 g of sodium hydroxide in 10 ml of alcohol was added. The sodium chloride which separated was filtered off, the alcohol distilled, the residue worked up with 100 ml of benzene, and filtered from a precipitate. The benzene solution was washed with a potassium carbonate solution, dried with potassium carbonate, and the benzene distilled. The residual oil was fractionated in vacuum. A fraction with b.p. 145-150° at 8 mm, weight 8.2 g (23.5% of theory) was obtained. It was a slowly crystallizing, colorless oil, readily soluble in many organic solvents.

10.768 mg substance: 28.61 ml 0.5 N $Na_2S_2O_3$. Found %: OC_2H_5 39.88. $C_{13}H_{17}O_2N$. Calculated %: OC_2H_5 41.07.

Aminomethylene-(phenyl)-acetonitrile. A solution of 11 g of methoxymethylene-(phenyl)-acetonitrile in 50 ml of absolute ethyl alcohol was saturated with ammonia at 0°. After standing for two days at 15°, the ammonia and the alcohol were removed in vacuum. The crystals were filtered, washed with cold absolute alcohol, and recrystallized from benzene. They were six-sided, somewhat extended platelets, m.p. 133-134°. They were readily soluble in alcohol, ether, acetone, and warm benzene, and insoluble in water. The substance was unchanged when heated for 3 hours to 150°.

5.150 mg substance: 7.14 ml 0.01 N H_2SO_4. Found %: N 19.41. $C_9H_8N_2$. Calculated %: N 19.44.

Ethyl aminomethylene-(phenyl)-acetate. A solution of 10 g of ethyl methoxymethylene-(phenyl)-acetate in 50 ml of methyl alcohol was saturated with ammonia at 0°. After standing for 5 days at 10-15°, the ammonia and the alcohol were removed in vacuum. The residual oil was vacuum distilled and a fraction with b.p. 142-143° at 3 mm, weight 6 g, was collected. It was readily soluble in the common organic solvents.

10.990 mg substance: 5.81 ml 0.01 N H_2SO_4. 6.843 mg substance: 3.65 ml 0.01 N H_2SO_4. Found %: N 7.40, 7.47. $C_{11}H_{13}O_2N$. Calculated %: N 7.33.

Diethyl-imino-bis-[methylene-(phenyl)-acetate]. A crystalline residue was obtained when a stream of dry hydrogen chloride was passed into a solution of 2 g of ethyl aminomethylene-(phenyl)-acetate in 15 ml of ether for 2 hours, followed by the removal of the hydrogen chloride and the ether in vacuum. When it was worked up with toluene, the insoluble part was filtered and identified as common salt.

The toluene was vacuum distilled and the residue dissolved in 10 ml of methanol. The next day the crystals were filtered and recrystallized from methanol several times until the melting point remained constant at 152-154°. They were large colorless platelets.

6.452 mg substance: 0.242 ml N_2 (19.5°, 730 mm). 7.817 mg substance: 12.66 ml 0.02 N $Na_2S_2O_3$. Found %: N 4.20; OC_2H_5 24.31. $C_{22}H_{24}O_4N$. Calculated %: N 3.84; OC_2H_5 24.64.

When the first methanol solution was evaporated to 3-4 ml and cooled, crystals melting at 122-124° after two methanol recrystallizations were obtained. Long needles.

8.678 mg substance: 0.306 ml N_2 (21.5°, 738 mm). 7.761 mg substance: 12.66 ml 0.02 N $Na_2S_2O_3$. Found %: N 3.97; OC_2H_5 24.48. $C_{22}H_{24}O_4N$. Calculated %: N 3.84; OC_2H_5 24.64.

Diethoxymethyl-(phenyl)-acetamide. 1.65 ml of purified thionyl chloride and 15.2 ml of dry pyridine were added at 20° to a solution of 10 g of diethoxymethyl-(phenyl)-acetic acid in 250 ml of absolute chloroform. After 5 minutes, the solution was diluted with 250 ml of chloroform, washed 2 times with 150 ml of a saturated sodium bicarbonate solution, 2 times with 200 ml of 1.0 N hydrochloric acid and 200 ml of saturated salt solution. The chloroform solution was then shaken for 15 minutes with 50 ml of 25% aqueous ammonia, washed 2 times with 50 ml of water, 2 times with 200 ml of saturated salt solution, and dried with sodium sulfate. The chloroform was vacuum distilled on the water bath. The residual crystals were twice recrystallized from toluene (1:5). Thin silky needles, m.p. 114-117°, weight 4 g.

7.053 mg substance: 0.381 ml N_2 (23.5°, 734 mm). Found %: N 6.01. $C_{13}H_{19}O_3N$. Calculated %: N 5.91.

Diethoxymethyl-(phenyl)-acetic acid was obtained on evaporating the aqueous ammonia solution to dryness, dissolving the residue in 50 ml of water, and acidifying carefully with 10% sulfuric acid. Weight 4.6 g, m.p. 118-119° after recrystallization from toluene (1:4). Diethoxymethyl-(phenyl)-acetamide could also be obtained by first preparing the mixed anhydride of diethoxymethyl-(phenyl)-acetic acid and benzoic or acetic anhydride and then heating it with aqueous ammonia. However, the yield was much lower.

Hydroxymethylene-(phenyl)-acetamide. A solution of 1 g of diethoxymethyl-(phenyl)-acetamide in 5 ml of concentrated hydrochloric acid was left at 0° for three hours. A white needlelike precipitate which separated, was filtered off, washed with concentrated hydrochloric acid, and dried in a vacuum desiccator over potassium hydroxide and sulfuric acid. Yield 0.7 g, m.p. 76-77° (decomp.). The substance was soluble in water and gave a violet coloration with ferric chloride solution.

The substance obtained was the hydrochloride of hydroxymethylene-(phenyl)-acetamide. All attempts to analyze the substance for chlorine gave unsatisfactory results, which indicated that the hydrochloride linkage with the amide group is unstable.

0.5 g of hydroxymethylene-(phenyl)-acetamide hydrochloride was mixed with 1 ml of water, 25 ml of ether, and 0.5 g of sodium bicarbonate. The substance dissolved in the ether. After drying with sodium sulfate and distilling the ether, the residue was recrystallized from a small amount of toluene; m.p. 99-101°; prisms. It was poorly soluble in cold water, readily in hot water, alcohol, toluene, and ether, and insoluble in petroleum ether. It gave a violet coloration with ferric chloride solution. It did not reduce silver. When it was dissolved in sodium hydroxide solution, it decomposed and a precipitate of phenylacetamide, m.p. 156° formed. It resembles hydroxymethylene-(phenyl)-acetic acid in its behavior toward bases.

4.868 mg substance: 0.363 ml N_2 (17.5°, 731 mm). Found %: N 8.43. $C_9H_9O_2N$. Calculated %: N 8.58.

α-(4-Carboxythiazolidyl-2)-phenylacetamide. 0.65 g of cysteine hydrochloride was added to a solution of 0.7 g of hydroxymethylene-(phenyl)-acetamide hydrochloride in 5 ml of dry pyridine. A solution formed on mixing, but soon became cloudy from a precipitate which was forming. After two days the crystals were filtered and washed with pyridine and dried in a vacuum desiccator over sulfuric acid; m.p. 149-150° (decomp.).

0.5 g of the substance was dissolved in 10 ml of water by the addition of several drops of 25% ammonia. The solution was filtered, cooled to 0°, and acidified with 10% sulfuric acid. Spherical clusters of needles separated slowly, were filtered off, washed with distilled water, and dried in a vacuum desiccator. The substance dissolved easily in water. It did not contain a free mercaptan group (reaction with ammonia and sodium nitroprusside). It decolorized 0.1 N iodine solution, which is characteristic for thiazolidine compounds; m.p. 172-173°.

8.118 mg substance: 0.706 ml N_2 (19°, 747 mm). 0.1530 g substance: loss on drying. 0.049 g. Found %: N 10.00; H_2O 3.2. $(C_{13}H_{14}O_3N_2S_2)H_2O$. Calculated %: N 10.19; H_2O 3.2.

SUMMARY

Derivatives of hydroxy-, alkoxy-, and aminomethylene-(phenyl)-acetic acid were prepared. Several peculiarities of this class of organic compounds were shown.

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* See Consultants Bureau translation, p. 1077.

XXI. THE QUANTITATIVE DETERMINATION OF SEVERAL NAPHTHALENE DISULFONIC ACIDS

A. A. Spryskov and B. I. Karavaev

The formation of four isomeric disulfonic acids upon sulfonation of naphthalene was already established in the 19th century. In 1864 Ufimtsev and Krivoshlikova [1] found the 1,7-isomer in the mixture of sulfonic acids, and, later, Chukasmma [2], the 1,3-isomer.

By the sulfonation of naphthalene to the disulfonic acids, a mixture consisting of 1,3-, 1,5-, 1,6-, 1,7-, 2,6-, and 2,7-isomers is obtained. However, the mixture obtained at lower temperatures apparently does not contain the 2,6-isomer, while that obtained at 140-160° does not contain the 1,5-isomer [3, 7]. A certain amount of mono- and trisulfonic acids is also produced during the sulfonation to the disulfonic acids.

The method for the determination of 2,6- and 2,7-disulfonic acids by means of the solubility of the mixture of the lead salts [4] cannot be used for the analysis of the sulfonation mixture. The method for the determination of the 1,5- and 2,6-isomers as barium and lead salts [3] has not been worked out. The methods for the determination of naphthalene 1,5-disulfonic acid by means of its m-xylidine salt and of the 1,6-acid as the β-naphthylamine salt [8] can be checked only in the absence of the 1,7-isomer, which is always present in the sulfonation mixture.

Korolev, Bilik, and Chuksanova [9] give two methods for the determination of 1,5-naphthalene disulfonic acid in a mixture with 1,6-naphthalene disulfonic acid and naphthalene trisulfonic acids, by saturation with benzidine and with sodium chloride. The methods were checked in the presence of 1,3-, 1,7-, and 2,7-isomers.

Ufimtsev and Krivoshlikova [1] give a method in which the sulfonic group is removed with oleum, followed by nitration and the reduction of the nitro compound. The relative amounts of the 1,6- and 1,7-disulfonic acids were determined in this manner. This type of method was used by Lantz [5], who nitrated the sulfonated mixture both in the cold and with heating. However, these methods of Lantz were tested in the absence of the 1,3- and the 1,7-isomers and were found to need many corrections, which had to be determined experimentally for each determination. The method for the determination of 1,5- and 1,6-isomers with the aid of amalgams [8] does not give satisfactory results.

The problem was to work out a method which could be used for the separate determination of the 1,5- and the 2,7-disulfonic acids in the presence of the 1,3-, 1,6-, and 1,7-isomers, and a method for the separate determination of the 2,6- and 2,7-disulfonic acids in the presence of the 1,3-, 1,6-, and 1,7-isomers, i.e., in sulfonation mixtures obtained at lower temperatures (to 120°) and at higher temperatures (from 140-165°).

As a basis for the method for the determination of the above isomers, their well known property of forming difficultly soluble salts with benzidine was used. The most difficultly soluble salts are the salts of the 2,6- and 1,5-acids, which are quantitatively precipitated under the conditions given below even at 60-65°. The benzidine salt of the 2,7-disulfonic acid dissolves somewhat more easily. It precipitates at 0°, although not quantitatively; and needs, for the determination of correct analytical results, the use of a constant correction.

EXPERIMENTAL

Analysis procedure. A sample of the pure sulfonic acids and sulfuric acid, or an approximately 1 g sample of the sulfonated mixture, was dissolved in 50 ml of water, the solution neutralized with 0.5 N caustic, and taken to a volume of 175 ml according to the mark on the beaker. 25 ml of a 10% barium chloride solution was added to the solution, which was heated to boiling, and then, after a few minutes, 50 ml of a benzidine hydrochloride solution (20 g of benzidine in 95 ml of hydrochloric acid, d 1.19, in 1 liter of water) was added to the hot solution, and it was once more heated to boiling. After cooling to 60-65°, the precipitated benzidine salts of the 1,5- or the 2,6-disulfonic acid were filtered, washed until a negative test for the chloride ion was given, transferred to a beaker, and titrated with 0.1 N alkali to phenolphthalein.

TABLE 1

Determination of the 1,5- and 2,7-isomers in artificially prepared mixtures

Used sulfonic acid in % of the total sulfonic acids							Found, in % of the total sulfonic acids		Error of the determination, in %	
1,5-	2,7-	1,6-	1,7-	1,3-	1,3,5-	α-	1,5-	2,7-	1,5-	2,7-
31.7	31.0	31.0	–	–	–	6.2	31.3	–	−0.4	–
56.5	10.3	16.5	–	–	–	16.6	55.2	–	−1.3	–
76.1	5.5	13.0	–	–	–	5.5	76.9	–	+0.8	–
40.2	52.0	7.8	–	–	–	–	40.2	52.6	0	+0.6
64.5	18.6	17.0	–	–	–	–	64.1	19.2	−0.4	+0.6
41.2	26.4	10.4	11.5	10.4	–	–	39.1	29.0	−2.1	+2.6
44.3	20.7	10.8	9.4	9.4	5.4	–	40.9	22.1	−3.4	+1.4
43.9	25.1	10.4	8.5	8.5	3.7	–	41.5	27.0	−2.4	+1.9
39.1	32.3	7.5	10.6	6.0	4.5	–	39.3	34.0	+0.3	+1.7

TABLE 2

Determination of the 2,6 and 2,7-disulfonic acids in artificially prepared mixtures (Expt. 1,2,5.9 in the presence of sulfuric acid)

Used sulfonic acid in % of the total sulfonic acids							Found, in % of the total sulfonic acids		Error of the determination, in %	
2,6-	2,7-	1,6-	1,3-	1,7-	1,3,6-	β-	2,6-	2,7-	2,6-	2,7-
7.4	50.2	30.7	–	–	–	6.5	7.1	–	−0.3	–
16.0	47.3	22.9	–	–	–	13.8	15.4	–	−0.6	–
31.6	53.8	14.6	–	–	–	–	32.6	55.1	+1.0	+1.3
19.9	66.0	14.1	–	–	–	–	20.7	69.1	+0.8	+3.1
22.6	50.4	9.0	9.0	–	–	9.0	23.2	50.4	+0.6	0
9.8	67.3	9.1	6.9	–	6.9	–	9.2	66.5	−0.6	−0.8
21.9	40.8	8.3	8.3	10.3	–	10.3	21.5	42.1	−0.4	+1.3
31.6	29.5	8.0	12.7	10.1	8.0	–	31.4	27.1	−0.2	−2.4
29.2	33.0	10.5	10.5	10.5	6.2	–	30.3	29.7	+1.1	−3.3

The filtrate from the benzidine salt was stored on ice. The benzidine salt of the 2,7-disulfonic acid which precipitated on standing was filtered off, washed free of chloride (five ml washes), transferred to a beaker, and titrated with 0.1 N alkali. The amount of 2,7-disulfonic acid was calculated by the formula $\frac{1.44a + 2.26}{s}$ = % 2,7-disulfonic acid, where a is the amount of 0.1 N alkali used for the titration, s — the weight of the analysis mixture; 2.26 — a correction for the incomplete precipitation of the 2,7-acid (found experimentally to be the average of 10 precipitation experiments). The amounts of the 1,5- and the 2,6-isomers were found with this formula, but without the correction factor.

The precipitation of the benzidine hydrochlorides of the naphthalene disulfonic acids (250 ml vol.) showed that the 1,5-acid was precipitated to an extent of 99%, the 2,6-acid, −100%, and the 2,7-acid −96.5% of the amount taken.

The results of the tests of the method for the determination of the 1,5- and the 2,7-isomers, which are given in Table 1, show that for artificially prepared mixtures of the pure sulfonic acids, the error for the determination of the 1,5-acid amounts to 2-3%, for the 2,7-acid −2.5%, and sometimes even more. The use of two parallel determinations is considered necessary. In the latter case the error for the determination will be less than 2%.

It must be pointed out that when the amount of the 1,5-isomer in the mixture is less than 0.1 g (i.e. if the amount of 0.1 N alkali for the titration of the benzidine salt falls below 7 ml), very inaccurate results are obtained; in this case the amount of the sample of the sulfonated mixture must be increased.

The data in the table also show that this method was checked even when all of the mono-, di-, and trisulfonic acids which can be found in preparations at lower temperatures (100-120°) are present in the mixture.

The results in Table 2 of the tests of the method for the determination of the 2,6- and 2,7-isomers in artificially prepared mixtures of the pure sulfonic acids (0.43-0.68 g mixtures) show that the error for the determination of the 2,6-acid amounts to 1.2%, and for the 2,7 acid, 3.0%. With two parallel analyses the error will not exceed 2%.

Table 3 contains the results of the testing of the method on sulfonation mixtures produced by the direct

TABLE 3

Determination of the 1,5- and the 2,7-disulfonic acids in the sulfonated mixture obtained at 40-60° and with the addition of the 1,5- and 2,7-isomers

Sulfonic acids in the sulfonated mixture				Amount of pure acids added to the sulfonated mixture		Resulting amount of the sulfonic acids in %		Found after the addition, in %		Error, in % of the total sulfonic acids	
In % of the total sulfonic acids			Total (g)								
1,5-		trisulfonic acids									
by the benzidine method	by the xylidine method	2,7-		1,5- (g)	2,7- (g)	1,5-	2,7-	1,5-	2,7-	1,5-	2,7-
50.5	49.0	0	6.2	0.3887	0.1784	0.1036	55.9	15.4	56.4	—	0.5	—
58.6	56.9	0	1.2	0.3499	0.1796	0.2322	50.5	30.6	51.8	27.2	1.3	3.4
54.3	55.5	0	1.4	0.3360	0.1455	0.1546	51.6	24.3	55.0	24.3	3.4	0
54.3	55.5	0	1.4	0.1680	0.1604	0.1426	53.4	30.3	54.2	33.1	0.8	2.8
54.3	55.5	0	1.4	0.1680	0.1745	0.1472	54.3	30.1	55.7	31.0	0.4	0.9

TABLE 4

Determination of the 2,6- and 2,7-disulfonic acids in the sulfonated mixture at 162° and with the addition of pure 2,6- and 2,7-isomers

Sulfonic acids in the sulfonated mixture				Amount of pure acids added to the sulfonated mixture		Resulting amount of the sulfonic acids in %		Found after the addition, in %		Error, in % of the total sulfonic acids	
In % of the total sulfonic acids			Total (g)								
		trisulfonic acids									
2,6-	2,7-			2,6- (g)	2,7- (g)	2,6-	2,7-	2,6-	2,7-	2,6-	2,7-
18.3	52.5	0.4		0.6462	0.0856	0.0798	25.1	51.7	25.2	53.1	0.1	1.4
19.0	50.0	0.4		0.6462	0.1663	0.2503	27.2	54.2	27.2	56.4	0.2	2.2

sulfonation of pure naphthalene. The naphthalene was sulfonated with pure 25% oleum for 4 to 9 hours at 40-60°. The solution of the sulfonated mixture was made up to 500 ml and titrated with an 0.1 N alkali solution to determine the amount of the di- and trisulfonic acids. The amount of the 1,5-disulfonic acid was determined by the above method and by means of its xylidine salt [6]. The 2,7-disulfonic acid was not detected in the mixture. The pure 1,5- and 2,7-disulfonic acids were added to the solution and the mixture reanalyzed for amounts of the 1,5- and 2,7-disulfonic acids.

The analysis results given in Table 3 show that the error of the determination sometimes amounts to 3.4% of the total sulfonic acids. As the table shows, two parallel runs give as an average more satisfactory results. The xylidine and benzidine methods give results in close agreement.

The results of the tests of the method for sulfonated mixture obtained by the sulfonation of 0.216 moles of naphthalene with 1 mole of CP 100% sulfuric acid for 6 hours at 162° are given in Table 4. The mixture gave a clear colorless solution when poured into water. After determination of the di- and trisulfonic acids by titration with 0.1 N alkali, the amounts of the 2,6- and the 2,7-isomers were determined by the above method. Then pure 2,6- and 2,7-disulfonic acids were added to the solution, which was then reanalyzed for the amounts of the 2,6- and 2,7-isomers. The results show the error for the determination of the 2,6-isomer is extremely small, and for the 2,7-isomer, using two parallel analyses, less than 2%.

The method for the determination of the 1,5-isomer as the m-xylidine salt [6] was studied in the presence of the 1,3- and the 1,7-isomers. The results show that the xylidine method gives good results even in the presence of the 1,3- and 1,7-acids, if the amount of the 1,5-isomer in the analytical sample is not less than 0.1 g.

The above method cannot be used for technical sulfonated mixtures [9]. It is still thought that the precipitation of the arylamine salts is hindered, not by the naphthalene trisulfonic acids, at least when they are present in small amounts, but by other impurities in the technical mixtures. The above method can be used for sulfonated mixtures obtained from chemically pure naphthalene and pure sulfuric acid or oleum, and can serve as a method for the study of processes for the preparation and isomerization of the disulfonic acids under various conditions.

SUMMARY

A very simple method for the determination of the amounts of the 2,6- and 2,7-naphthalene disulfonic acids in sulfonated mixtures obtained at high temperatures (140-165°) by means of their benzidine salts is given.

The method given earlier [9] for the determination of the 1,5-isomer by means of its benzidine salt was worked out and tested for the determination of the 1,5- and the 2,7-disulfonic acids in mixtures obtained at lower temperatures (to 120°).

The error for the determination of the 2,6-disulfonic acid does not exceed 1%, and the error for the determination of the 1,5- and 2,7-isomers with two parallel analyses does not exceed 2% of the total sulfonic acids.

The determination is made by a macro method and consumes little time.

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XXIII. PREPARATION OF THE ACID CHLORIDES AND OTHER DERIVATIVES OF THE NAPHTHOL DISULFONIC ACIDS

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The acid chlorides of the sulfonic acids are important not only for the identification and purification of the sulfonic acids, but also for the preparation of their derivatives. The existence of many known naphthol sulfonic acids makes their acid chlorides important for the achievement of the first and second aim. However, their preparation from the salts of the sulfonic acids by means of phosphorus chlorides is not possible; instead the phenolic hydroxyl is substituted by chlorine. The attempts of Claus and Mielcke [1] as well as Holt and Mason [7] in this direction cannot be considered successful, since the chlorides were not obtained in crystalline form.

The action of chlorosulfonic acid on 1- and 2-naphthols or naphthol monosulfonic acids leads to the formation of a mixture of disulfonyl chlorides and trisulfonyl chlorides. For example, a mixture was obtained from 1-naphthol and chlorosulfonic acid from which 1-naphthol-2,4-disulfonyl chloride [2], and 1-naphthol-2,4,7-trisulfonyl chloride were isolated. The action of chlorosulfonic acid on 2-naphthol produces a mixture from which 2-naphthol-1,6-disulfonyl chloride and 2-naphthol-1,5-disulfonyl chloride were isolated. By increasing the temperature, 2-naphthol-3,6,8-trisulfonyl chloride [2] may be obtained. 2-Naphthol-6-sulfonic acid and 2-naphthol-1-sulfonic acid give 2-naphthol-1,6-disulfonyl chloride when treated with chlorosulfonic acid [3]. 2-Naphthol-6,8-disulfonyl chloride is obtained from 2-naphthol-6-sulfonic acid. 2-Naphthol-1,5-, 2-naphthol-1,6- and 2-naphthol-1,7-disulfonyl chlorides may be obtained by the action of chlorosulfonic acid upon 2-naphthol-5-sulfonic acid, 2-naphthol-6-sulfonic acid, and 2-naphthol-7-sulfonic acids, respectively [4]. 1-Naphthol-2,4,7-trisulfonyl chloride can be obtained by the action of chlorosulfonic acid upon 1-naphthol-2-, 1-naphthol-4-, or 1-naphthol-7-monosulfonic acids [5], or on 1-naphthol-2,4- and 1-naphthol-2,7-disulfonic acids [6]. 1-Naphthol-4,6,8-trisulfonyl chloride is obtained from 1-naphthol-4,6- and 1-naphthol-6,8-disulfonic acids.

The claim of Steinkopf that 2-naphthol-3,6-disulfonyl chloride could be obtained by the action of chlorosulfonic acid upon Schaeffer's salt is erroneous. As has been shown by Pollak [3], Steinkopf obtained 2-naphthol-1,6-sulfonyl chloride, m.p. 111°.

The preparation of the naphthol sulfonyl chlorides by the action of chlorosulfonic acid on the salts of the corresponding sulfonic acids without the introduction of new sulfonic groups is not reported in the literature except for the preparation of sultone-sulfonyl chlorides from the salts of 1-naphthol-3,8- and 1-naphthol-4,8-disulfonic acids [6].

The mono amides of 1-naphthol-3,8- and 1-naphthol-4,8-disulfonic acids were obtained by the action of ammonia on the sultones. Almost nothing is given about the properties of these amides (for example their melting points) [9]. Holt and Mason [7] claim the preparation of 2-naphthol-3-sulfonamide; however, its analysis is not given, and its formation by the method given can be doubted. Finally, the preparation of 2-naphthol-6-sulfonamide from 2-hydroxy-6-chlorosulfoxy-1-naphthoic acids [8] must be mentioned.

The method for the preparation of naphthol disulfonyl chlorides by the action of chlorosulfonic acid upon the salts of the corresponding sulfonic acids was studied in the present work. Some amides and anilides of the naphthol disulfonic acids were also obtained.

EXPERIMENTAL

The work was conducted on two α-naphthol disulfonic acids (1,3,8- and 1,4,8-) and on two β-naphthol disulfonic acids (2,6,8- and 2,3,6-).

The derivatives of 1-naphthol-4,8-disulfonic acid. Technical sodium salt (Khalbaum) was used to prepare the acid chloride of 1-naphthol-4,8-disulfonic acid. It gave a salt, m.p. 187°, instead of 205° given in the

TABLE 1

Preparation of 1-naphthol-4,8-disulfonyl chloride by the reaction of the sodium salt of the acid with chlorosulfonic acid at 20° for 24 hours

Expt. No.	Materials taken			Yield of the chloride (in % of theoretical)	Melting point of the chloride	
	Salt of the naphthol-sulfonic acid, g	HSO_3Cl (in ml)	HSO_3Cl moles per 1 SO_3Na group		Crude	Once recrystallized
154	12	46	10	64.2	185°	197°
155	25	100	10	50.4	185	197
162	60	200	8	43.0	185	193
166	35	100	8	50.0	175	—

literature, with benzylisothiourea [12]. After one recrystallization, the melting point of the salt rose to 196° (without correction). Thus an impure salt was being used.

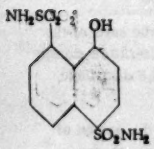
While the reaction vessel was cooled with cold water, the sodium salt was mixed with chlorosulfonic acid (redistilled at atmospheric pressure), and the mixture kept at room temperature (about 20°) without stirring for 24 hours. After the mixture was poured on ice, the chloride was filtered off, washed with ice water, and dried in a vacuum desiccator over sodium hydroxide sticks. The results of the experiments, listed in Table 1, show that the chloride was obtained in an average yield of slightly more than 50% of theory. The increase of the reaction time to 72 hours or the increase of the temperature to 60° did not improve the yield of the chloride.

The crystalline chloride obtained was not soluble in water, difficultly soluble in alcohol, and soluble in benzene. For recrystallization, the product was dissolved in benzene by warming, and after the addition of 1/4 volume of ether, cooled with ice and salt. A product, m.p. 197°, was obtained by one recrystallization in most cases. A second and third recrystallization did not raise the melting point. The amount of chlorine in the product indicated that it was the acid chloride sultone (I).

(I)

The product was analyzed by boiling with alkali and titrating by the Volhard method.

A considerable amount of the chloride remained unchanged after it was reacted with concentrated ammonia for 0.5 hours at 50-60°. After standing at room temperature for two days with the ammonia, the chloride dissolved completely. Apparently, the hydrolysis of the chloride, with the formation of the ammonium salt of the disulfonic acid, occurred. When dry ammonia was passed for one hour into a 3-5% solution of the chloride in benzene, a yellow precipitate formed, which consisted of a mixture of ammonium chloride and 1-naphthol-4,8-disulfonamide (II). The amide, unreported in the literature, was insoluble in benzene, ether, carbon disulfide, and dichloroethane.



(II)

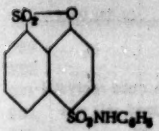
To separate the ammonium chloride from the amide, the mixture was twice dissolved in a small amount of water and filtered. The amide obtained did not contain any chloride ion or sulfonyl chloride and, even after boiling it with alkali, no chloride ion could be detected. The amide dissolved in water and alcohol, but could not be crystallized from them. The only way it could be purified was to dissolve it in alkali or in ammonia and precipitate it with acid to give a fine crystalline product. When it was treated with 10% alkali in the cold, saponification did not take place, and only at 60-70° did any energetic separation of ammonia occur. The product, which was dried in a desiccator, melted at 170-210°. After it was dried at 130°, the product lost 4.9% of its weight, but the melting point remained spread out. The amount of nitrogen in the product (7.95%, instead of the 9.26% calculated for $C_{10}H_{10}O_8N_2S_2$) also showed that it either contained water of crystallization or was not homogeneous.

The ammonia salt of the sulfonic acid, obtained by saponifying the chloride in dilute alkali, evaporating the solution to dryness, and neutralizing with ammonia, was recrystallized from water, forming platelets with m.p. 275-277°.

Upon heating the chloride of the sulfonic acid sultone with 4 moles of aniline in benzene solution for 30-40 minutes at temperatures not higher than 70°, followed by a 3 hour stay at 40°, aniline hydrochloride separated out. After filtering it off, the filtrate was evaporated in vacuum to half its volume. A crystalline precipitate, silver white scales, m.p. 145°, amounting to 30-40% of the chloride used, precipitated overnight. The melting point did not change after two recrystallizations from alcohol. The product did not dissolve in cold water, dissolved only slightly in hot water, and moderately in alcohol; it was very soluble in benzene, ether, and dichloroethane. The product appears to be the sultone sulfanilide (III).

0.7786 g substance: 21.79 ml 0.1 N HCl. Found %: N 3.87 (Kjeldahl). $C_{16}H_{11}O_3NS_2$. Calculated %: N 3.88.

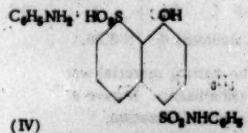
If the benzene solution, after the preparation of the anilide, was filtered from the aniline hydrochloride, the benzene evaporated, and the residue dissolved in alkali, then a rupture of the sultone ring occurred and the sultone sulfanilide was changed to the sodium salt of 1-naphthol-4-sulfanilid-8-sulfonic acid, which was easily soluble in water. The aniline salt of 1-naphthol-4-sulfanilid-8-sulfonic acid (IV) separated when this solution, which contained aniline, was acidified with hydrochloric acid.



(III)

It was poorly soluble in cold water, but very soluble in hot water. It dissolved well in alcohol, and was not soluble in benzene and dichloroethane. The melting point, after more than one recrystallization from water, was 197°.

0.9643 g substance: 40.66 ml 0.1 N HCl. 0.7237 g substance: 30.53 ml 0.1 N HCl. Found %: N 5.91, 5.90. $C_{22}H_{16}O_5N_2S_2$. Calculated %: N 5.93.



(IV)

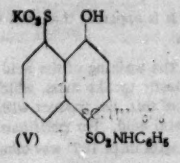
The salt could be titrated with 0.1 N alkali in the presence of phenolphthalein. The results were better if an aliquot of the alkali was added to the salt and then back titrated with 0,1 N acid.

0.1418 g substance: 2.98 ml 0.1 N NaOH. Found: M 475.1. $C_{22}H_{16}O_5N_2S_2$. Calculated: M 472.3.

If the sultone of 1-naphthol-4-sulfanilid-8-sulfonic acid, m.p. 145°, was dissolved in potassium hydroxide and acidified with hydrochloric acid in the absence of aniline, then the potassium salt of 1-naphthol-4-sulfanilid-8-sulfonic acid (V), separated. It was recrystallized from water and had a m.p. of 231-232°.

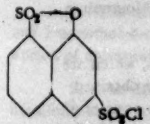
0.3234 g substance: 7.57 ml 0.1 N HCl. 0.1262 g substance: 0.0248 g K_2SO_4. Found %: N 3.32; K 8.82. $C_{16}H_{12}O_6NS_2K$. Calculated %: N 3.35; K 9.36.

The derivatives of 1-naphthol-3,8-disulfonic acid. The starting material was the technical sodium 1-naphthol-3,8-disulfonate of Kahlbaum, which was identified by its change to the sultone sulfonic acid upon heating it with sulfuric acid. The sultone sulfonic acid obtained melted at 240°. According to the literature, the melting point of the sultone sulfonic acid is 241° [11]. For the preparation of the acid chloride, the salt was mixed with redistilled chlorosulfonic acid and kept at room temperature for 24 hours. The mixture was then poured on ice, filtered off, washed, and dried in a vacuum desiccator. The results of the experiments, listed in Table 2, show that a yield of 88% was obtained from the once recrystallized salt. The crude chloride crystallized well from dichloroethane. After three recrystallizations, the melting point remained constant at 187-188°. The product was the sultone sulfonyl chloride (VI).



(V)

0.1828 g substance: 5.87 ml 0.1 N $AgNO_3$. Found %: Cl 11.39. $C_{16}H_9O_5S_2Cl$. Calculated %: Cl 11.64.



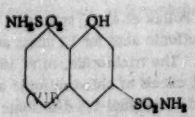
(VI)

Upon passing dry ammonia into a 3-5% solution of the chloride in dichloroethane, the amide precipitated almost quantitatively. It was insoluble in benzene, ether, carbon disulfide, and dichloroethane. It was moderately soluble in alcohol and water. The amide was purified by dissolving it in alkali and reprecipitating it with hydrochloric acid. The amide melted at 226-227° after drying at 120°.

0.5107 g substance: 30.31 ml 0.1 N HCl. Found %: N 8.88. $C_{16}H_{13}O_5N_3S_2$. Calculated %: N 9.26.

Therefore the product appears to have been 1-naphthol-3,8-disulfondiamide (VII).

The anilide of 1-naphthol-3,8-disulfonic acid was obtained by mixing a benzene solution of the sultone sulfonyl chloride (3.5 g in 100 ml) and aniline (4.05 g). When the solution was heated slightly, aniline hydrochloride separated. It was filtered after standing overnight, and the benzene distilled from the filtrate. The residue was recrystallized twice from alcohol over charcoal, and white crystals m.p. 213-213.5°, were obtained (VIII). The



(VII)

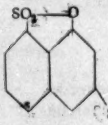
TABLE 2

Preparation of the chloride of 1-naphthol-3,8-disulfonic acid by the treatment of its sodium salt with chlorosulfonic acid at 15-20° for 24 hours

Expt. No.	Materials taken			Yield of the chloride (in % of the theoretical)	Melting point of the chloride		Notes
	Salt of the naphthol disulfonic acid (in g)	HSO_3Cl (ml)	HSO_3Cl moles per 1 SO_3Na group		Crude	Once recrystallized	
158	12	48	10.5	66.6	170-172°	—	
191	25	140	14.6	60.0	173-175	187°	
202	14.5	60	10.8	86.5	173	185	A once recrystallized salt was used

anilide obtained was soluble in alcohol, benzene, and ether, and poorly in water.

0.3292 g substance: 8.83 ml 0.1 N HCl. Found %: N 3.75. $C_{16}H_{11}O_5NS_2$. Calculated %: N 3.88.



(VIII)

The derivatives of 2-naphthol-6,8-disulfonic acid. The starting material was the technical sodium salt of 2-naphthol-6,8-disulfonic acid (Khalbaum). It gave a salt with m.p. 210-215° with benzylisothiourea, which, after recrystallization, melted at 220-221°.

For the preparation of the acid chloride, the sodium salt was mixed in the cold with redistilled chlorosulfonic acid, and the mixture heated for some time. Then it was poured on ice, washed by decantation, and filtered. The results of the experiments, listed in Table 3, show that the optimum conditions for the preparation of the chloride were to keep the reaction mixture for 2 hours at about 78° or somewhat lower.

It is apparent that with temperatures higher than the above, sulfonation took place, forming the trisulfonyl chloride.

The washing of the acid chloride on the funnel was very difficult because when it was squeezed it turned into a plastic tarlike mass, which only turned to a powder on drying in a desiccator or in the oven at 50-60°. Because of this, the product with the melting points listed in Table 3 still had not been completely freed of the mineral acid. For purification, the chloride was dissolved in benzene and precipitated with gasoline; a product with m.p. 157° was obtained. A recrystallization was needed to obtain the pure product, m.p. 161-162° [3].

When dry ammonia was passed into a benzene solution of the chloride, the amide precipitated. It was dissolved in alkali and reprecipitated with acid from the basic solution. The product did not contain chlorine and gave off ammonia when it was warmed with alkali.

The action of chlorosulfonic acid on 2-naphthol-3,6-disulfonic acid. Sodium 2-naphthol-3,6-disulfonate, purified by precipitation by alcohol from water, was used for the experiments. It gave a benzylisothiouronium salt, m.p. 233°. The same melting point is given in the literature for this salt [12].

The results of the reaction of the R-salt with chlorosulfonic acid, followed by pouring on ice, which are listed in Table 4, show that the chloride could not be obtained at lower temperatures. The chloride obtained at temperatures of 60-100° after one recrystallization from dichloroethane, had m.p. 170°, and after a series of recrystallizations, had m.p. 175°. When it was analyzed by titration of the base after saponification for chlorine content, it was shown that the trisulfonyl chloride had formed.

0.1255 g substance: 0.1190 g AgCl. 0.1048 g substance: 14.01 ml 0.1 N NaOH(after saponification). Found %: Cl 23.46; M 448.7. $C_{10}H_5O_7S_3Cl_3$. Calculated %: Cl 24.22; M 439.4.

Pollak et al [2] state that when 2-naphthol-3,6-disulfonic acid was treated with a ten-fold quantity of chlorosulfonic acid for 12 hours at room temperature, 2-naphthol-3,6,8-trisulfonyl chloride, m.p. 196°, was formed. The trichloride, m.p. 196°, was also isolated from the product of the reaction of 2-naphthol with a ten-fold excess of chlorosulfonic acid at 130-140° for 2.5 hours. The same chloride was obtained from 2-naphthol-1,5- and 2-naphthol-1,6-disulfonic acids, and 2-naphthol-3,6,8-trisulfonic acid at 130°.

TABLE 3

Preparation of the chloride of 2-naphthol-6,8-disulfonic acid by treating its sodium salt with chlorosulfonic acid

Expt. No.	Material used		Reaction temperature	Duration (in hours)	Chloride obtained	
	Salt of the naphthol disulfonic acid (in g)	HSO_3Cl (in ml)			Melting point	Yield (in % of theoretical)
229	4	16	16°	19	–	Low
239	4	16	40	6	133°	38.3
231	4	13	45-55	6	139	51.5
230	4	16	45-55	6	146-147	58.0
238	4	16	78	2	146	57.5
254	20	100	78	2	144-145	73.0
242	4	16	100	2	100-105	75.1

The acid chloride obtained is apparently 2-naphthol-1,3,6-trisulfonyl chloride, as was shown by the following. 2-naphthol-1,6-disulfonyl chloride, m.p. 111° [3], was obtained from 2-naphthol-6-sulfonic acid. When 2.2 g of this was heated with 9 ml of chlorosulfonic acid for 2 hours to 100°, a product with m.p. 152° was obtained. After recrystallization from dichloroethane and carbon disulfide, a product with a constant m.p. of 176.5° was obtained. A mixed melting point determination with the products obtained in Experiments 251, 243, and 244 gave no depression.

TABLE 4

The action of chlorosulfonic acid on sodium 2-naphthol-3,6-disulfonate

Expt. No.	Materials taken		Reaction temperature	Duration (in hours)	Chloride		
	R-Salt (g)	HSO_3Cl (ml)			Yield (in % of theoretical)	Melting point	
						Crude product	Recrystallized product
263	2.2	14	Room	18	No precipitate on ice		
262	2	20	Room	60	Precipitate melted in the air		
240	4	16	40°	6	Very little precipitate		
248	4	16	61	2	43	75-96°	–
251	4	16	61	6	45.2	130-135	169-171°
244	7	28	65-70	2	34	~ 138	175
241	4	16	78	2	43.8	~ 138	166-168
243	4	16	100	2	57.5	144-148	171

SUMMARY

1. The methods for the preparation of the sultones of 1-naphthol-3-sulfonylchloride-8 sulfonic acid, and 1-naphthol-4-sulfonyl-chloride-8-sulfonic acid, and 2-naphthol-2,6-disulfonyl chloride by means of the action of chlorosulfonic acid on the sodium salts of the corresponding naphthol sulfonic acids were studied.

2. The diamides of 1-naphthol-3,8-disulfonic acid, 1-naphthol-4,8-disulfonic acid, and 2-naphthol-6,8-disulfonic acid have been obtained for the first time.

3. The sultones of 1-naphthol-3-sulfonyl chloride-8-sulfonic acid and 1-naphthol-4-sulfonylchloride-8-sulfonic acid as well as the aniline and potassium salts of 1-naphthol-4-sulfanilid-8- sulfonic acid have been obtained for the first time.

4. 2-Naphthol-1,3,6-trisulfonyl chloride was obtained by the action of chlorosulfonic acid on 2-naphthol-3,6-disulfonic acid at 60-100°.

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RESEARCHES ON AMINO ACIDS

I. THE SYNTHESIS OF β-ALANINE

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The ability of acrylonitrile to add amines, amides, acids and other compounds to its double bond has been used for the synthesis of a whole series of valuable products [1]. β-Alanine is among these. There are several methods for preparing β-alanine from acrylonitrile. When acrylonitrile is heated with a concentrated aqueous ammonia solution, aminopropionitrile is obtained [2]. This gives β-alanine on hydrolysis. The method of preparing β-alanine from acrylonitrile by condensation with phthalamide, followed by saponification of the resulting phthalamidopropionitrile is interesting [3]. Because of the work of V. M. Rodionov and N. G. Yartseva, who employed an easily prepared catalyst for the condensation reaction of acrylonitrile and phthalamide, this method of preparing β-alanine became more feasible [4]. These authors also give an original method for separating β-alanine from its hydrochloride [5].

Among many methods unsatisfactory for various reasons [6], there is a method for preparing β-alanine from β-iodopropionic acid [7]. Certainly β-iodopropionic acid cannot be a convenient raw material for β-alanine, but the possibility of using β-halopropionic acid for the preparation of β-alanine was investigated in the present work.

In the place of iodopropionic acid, β-chloropropionic acid obtained in good yield by heating acrylonitrile and hydrochloric acid, was used.

$$CH_2{=}CH{-}CN \xrightarrow{HCl} \underset{Cl}{CH_2{-}CH_2{-}COOH} \xrightarrow{NH_3} \underset{NH_2}{CH_2{-}CH_2{-}COOH}.$$

When β-chloropropionic acid is reacted with aqueous ammonia, the halogen atom is replaced by an amino group and β-amino propionic acid (β-alanine) is formed. After distillation of the ammonia solution, it separates in a mixture with iminodipropionic acid. β-Alanine is obtained in 50% yield from this mixture. When iminodipropionic acid is fused with phthalic anhydride, β-phthaloylaminopropionic acid, which can be used in the synthesis of pantothenic acid [4], is formed. By saponifying β-phthaloylaminopropionic acid, about 6% more of the theoretical amount of β-aminopropionic acid can be obtained.

EXPERIMENTAL

β-Chloropropionic acid was obtained according to the method in the patent literature [8], by heating acrylonitrile with hydrochloric acid, with yields of 82-85% of theory.

β-Alanine. 200 g (92%) of β-chloropropionic acid was dissolved in 4 liters of 22% ammonia solution and allowed to stand for 10-12 days. At the end of this period, 10 g of charcoal was added to the solution, which was filtered and evaporated to dryness in vacuum. 0.5 liter of conc. hydrochloric acid was added to the residue, and the mixture was boiled for 0.5 hours. The hydrochloric acid solution was evaporated in vacuum, and after removal of the hydrochloric acid, water was added twice to the residue and evaporated to dryness. The residue was freed of the last traces of moisture in a vacuum desiccator over phosphorus pentoxide. This dried residue was extracted with boiling 96% alcohol (500 ml) cooled, and filtered. The filtered salt was heated with 350 ml of 96% alcohol, filtered, and the filtrate combined with the first alcohol extract. 103 g of diethylamine was then slowly added until a pH of 7.6 was obtained. Small white crystals of β-alanine separated. On the following day, the crystals were filtered, washed three times with alcohol (50 ml) and dried. 71 g of β-alanine, m.p. 189-195°, was obtained. The alcoholic mother liquor and washings were evaporated to a volume of 200 ml and the semi-solid residue pressed carefully on the funnel in order to remove the bulk of the diethylamino hydrochloride. The filtrate was evaporated to dryness in vacuum and treated with 1.2 liters of cold chloroform, which dissolved everything except 34 g of a yellowish oil. This oil was once more triturated with a small amount of chloroform and the chloroform added to the main solution. The oil was allowed to stand and it crystallized completely (residual

β-alanine). 36% sodium hydroxide was added to the residue from the removal of the chloroform in vacuum and the diethylamine distilled.*

The basic solution freed from the diethylamine, was evaporated and the residue boiled with concentrated hydrochloric acid. After removal of the hydrochloric acid and the twice-added water in vacuum, the residue was extracted with alcohol. 4.5 g of β-alanine was isolated from the alcoholic extracts with diethylamine. The mother liquor, after the removal of the 4.5 g of β-alanine, was processed in the same way as the mother liquor after the removal of the first batch of β-alanine, and 3 g more was obtained. A total of 78.5 g of technical β-alanine was obtained.

For purification it was dissolved in the minimum amount of water and precipitated with eight volumes (in respect to the water) of alcohol. It was filtered, washed, and dried. More β-alanine was obtained after the evaporation of the alcohol-water solution, and the residue reprecipitated once more from water with alcohol. A total of 76.5 g, 50.6% of the theoretical amount, of β-alanine, was obtained; m.p. 195-197°.

Found %: C 40.24; H 8.10; N 15.70. $C_3H_7O_2N$. Calculated %: C 40.45; H 7.86; N 15.73.

Derivatives of iminopropionic acid were obtained from the 34 g of the oily product.

Diethyl iminodipropionate. A stream of dry hydrogen chloride was passed for 4 hours in the cold into a suspension of 22.4 g of the oil and 80 ml abs. alcohol. The oil slowly dissolved and the reaction mixture was boiled for 4 hours. The solution was evaporated in vacuum and the residue dissolved in 50 ml of water. Ether was added to the solution and it was carefully mixed with 30% sodium hydroxide until it was strongly alkaline. The ether was separated and the basic solution extracted several times with ether. The combined ether extracts were dried with fused sodium sulfate, and the ether removed. The residue was fractionated in vacuum at 15 mm. The fraction, up to 145°, did not contain any amino derivatives. Diethyl iminodipropionate hydrochloride was obtained from the fraction, b.p. 145-147°. 3.65 g of the ester was dissolved in 3 ml of absolute alcohol and treated with alcoholic hydrogen chloride until acid on Congo. Diethyl iminodipropionate hydrochloride was precipitated from this solution with dry ether as large colorless plates. After recrystallization from ethyl acetate, diethyl iminodipropionate hydrochloride melted at 78-79°.

Found %: N 5.77; Cl 13.80. $C_{10}H_{20}O_4NCl$. Calculated %: N 5.52; Cl 13.99.

β-Phthaloylaminopropionic acid. 11.4 g of the oil and 10.5 g of the phthalic anhydride was heated in a flask to 180-202° for 30 minutes. Acrylic acid and water distilled during the reaction. On cooling, the contents of the flask were dissolved in 60 ml of methanol and cooled. The precipitated crystals were filtered off and recrystallized once more from 60% methanol. The β-phthaloylaminopropionic acid obtained melted at 150-151°.

Found %: C 60.56; H 3.94; N 6.47. $C_{11}H_9O_4N$. Calculated %: C 60.27; H 4.11; N 6.39.

SUMMARY

1. β-Alanine was obtained in 50-56% yield by the reaction of β-chloropropionic acid with aqueous ammonia.

2. β-Alanine can be obtained from the hydrochloride by means of diethylamine.

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* The distilled diethylamine and the diethylamine obtained earlier from the hydrochloride were dried with caustic and distilled. A 60% recovery of the diethylamine was obtained.

SPECTROPHOTOMETRY OF BIURET COORDINATION COMPOUNDS AS A METHOD OF INVESTIGATION OF PROTEINS AND PEPTIDES

XIV. INFLUENCE OF THE AMINO ACID COMPOSITION OF THE PEPTIDES ON THE CHARACTER OF LIGHT ABSORPTION BY BIURET COORDINATION COMPOUNDS

M. I. Plekhan

The previous studies of the copper biuret coordination compounds of proteins [1-5] led to the conclusion that the properties of these complexes greatly resemble those of the coordination compounds of the tripeptides (diglycylglycine) and differ greatly from the coordination compounds of long-chain peptides. There was, however, a slight shift in the absorption maximum (10-15 mμ) of the protein coordination compounds toward the shorter wavelengths, suggesting the presence of some "red" complexes as impurities. This phenomenon can indicate the presence of a small amount (5-10%) of tetrapeptide in the protein molecule, along with the main mass of the tripeptides. Another explanation, however, is more probable. The tripeptide chains of the protein molecules, containing more complex amino acids than the simple tripeptide diglycylglycine, form coordination compounds with absorption maxima shifted toward the shorter wavelengths. This hypothesis could only be verified experimentally. It was necessary to explain the influence of the amino acid content of peptides on the biuret reaction. There is almost no data in the literature on this question.

The study of the biuret reaction of the polypeptides can be very complex because a large amount of peptides can be formulated by the permutation of the known amino acids. It was considered hardly expedient to run this volume of experiments, because of the concurrent great amount of experimental difficultly connected with the preparation of this great number of peptides and the improbability of its achievement.

For the present the study was limited to model di- and tripeptides in which one amino acid was made to be the carrier of the property to be studied. In this way, it was easier to establish the effect of each amino acid on the character of the coordination compound formation. In particular, bearing in mind the absorption spectrum of the glycyl tripeptide, it was of interest to determine the particular absorption which occurred when one of the glycine groups was changed to another amino acid. The following di- and tripeptides were prepared and studied: 1) glycylglycylthreonine; 2) leucylglycylasparagine; 3) leucylglycyltryptophan; 4) alanylglycylglycine; 5) carbobenzoxydiglycylglycine; 6) glycylthreonine; 7) glycylasparagine; 8) glycyltryptophan; 9) leucylhistidine; 10) glycyltyrocine; 11) carbenzoxyglycylglycine.

TABLE 1

Amount of copper in the mixed amino acid tripeptide biuret complexes

Expt. No.	Tripeptide	Amount of copper per mole of peptide (in g)	(in moles)
1	Glycylglycylglycine	61.6	0.97:1
2	Alanylglycylglycine	57.82	0.90:1
3	Leucylglycyltryptophan	65.8	1.03:1
4	Leucylglycylasparagine	52.9	0.83:1
5	Glycylglycylthreonine	44.0	0.69:1

1. Copper Biuret Coordination Compounds of the Tripeptides

Solutions of the biuret coordination compounds were prepared in the usual manner (see the Experimental section).

The iodometric determination of copper in the peptide coordination compounds gave the following results, listed in Table 1.

The characteristic ratio between the copper and the peptide is equal to 1:1 for the first four tripeptide coordination compounds. The amount of copper in the glycylglycylthreonine complex is considerably lower than in all of the other complexes studied.

Spectrophotometric measurement of the absorption of light by the tripeptide copper coordination compounds showed that the influence of the various amino acids on the character of the absorption by the complex was far from being the same. Table 2 and Figure 1 contain the results of these measurements.

Analysis of the data obtained indicates the following:

1) A change of one of the glycine residues in the glycyl tripeptide to an alanine exerts an insignificant effect on the coordination compound; the position of the absorption maximum remains at the same wavelength [575 mμ] as in diglycylglycine, but the intensity of the absorption increases somewhat.

2) The introduction of asparagine into the tripeptide sharply changes the character of the coordination compound formation, a "red" coordination compound being formed, whose absorption maximum is the wavelength 525 mμ. Compared to the glycyl tripeptide coordination compound, the absorption maximum of leucylglycylasparagine is shifted towards the lower wavelengths by 50 mμ.

TABLE 2

Optical Density of the tripeptide copper biuret complexes (1/150 molar solutions)

No.	Wavelength λ (in mμ)	Magnitude of the optical density ε					
		Diglycyl-glycine	Glycyl-glycyl-threonine	Leucyl-glycylas-paragine	Leucyl-glycyl-tryptophan	Anamyl-glycyl-glycine	Carbobenz-oxydiglycylglycine
1	480	0.222	0.233	0.325	0.336	0.212	0.066
2	505	0.310	0.341	0.425	0.472	0.310	0.108
3	520	0.360	0.387	0.458	0.526	0.384	0.137
4	525	—	—	0.458	—	—	—
5	530	0.392	0.407	0.458	0.550	0.435	0.155
6	535	—	0.410	0.451	—	—	—
7	540	0.416	0.412	0.445	0.564	0.480	0.168
8	545	—	0.411	—	—	—	—
9	550	0.442	0.411	0.428	0.578	0.520	0.177
10	560	0.451	0.405	0.402	0.589	0.550	0.179
11	570	0.460	0.393	0.371	0.595	0.565	0.176
12	575	0.463	—	—	0.596	0.570	—
13	582	0.443	0.378	0.334	0.597	0.562	0.171
14	585	—	—	—	0.596	—	—
15	595	—	—	—	0.590	—	—
16	600	0.423	0.344	0.278	0.584	0.550	0.152
17	610	0.393	0.322	0.248	0.570	0.499	0.142
18	620	0.374	0.299	0.216	0.545	0.447	0.128
19	630	0.351	0.272	0.188	0.514	0.417	0.106
20	640	0.330	0.243	0.161	0.482	0.365	0.093
21	650	0.313	0.215	0.140	0.441	0.318	—
22	670	0.280	0.158	0.100	0.358	0.224	0.081
23	693	0.240	0.107	0.067	0.264	0.138	0.039
24	710	0.191	0.078	0.050	0.200	0.090	0.031
25	730	0.134	0.054	0.036	0.146	0.060	0.025

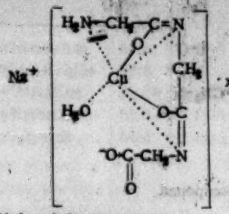
3) The introduction of threonine into the tripeptide molecule (glycylglycylthreonine) shifts the absorption maximum of the complex strongly toward the shorter wavelengths (540 mμ). The absorption is of mixed character lying between the absorption of the "red" and the "violet" coordination compounds. Compared to the glycyl tripeptide coordination compound, the maximum is shifted by 30 mμ.

4) The appearance of tryptophan in the tripeptide shifts the maximum slightly (by 7 mμ) toward the longer wavelengths (it lies at 582 mμ) and the intensity of the absorption is somewhat increased.

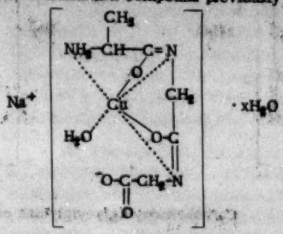
5) The change of one of the hydrogen atoms in the amino group of diglycylglycine to the carbobenzoxy group, shifts the absorption maximum of the complex by 15 mμ towards the shorter wavelengths [560 mμ].

Therefore, on the basis of these results an important conclusion can be drawn. The functional groups of the amino acids which make up the tripeptides enter into the formation of coordination compounds and exert specific influences on the character of the absorption. The entrance of alanine into the tripeptide does not shift the absorption maximum of the coordination compound, but only increases somewhat the intensity of the absorption. This indicates that the character of the bonds which determine the resulting absorption spectrum of an alanylglycylglycine coordination compound are the same as in the diglycylglycine complex. The plain CH_3 radical, as expected, does not form a bond with the copper atom, but the increase in the molecular volume leads to the increased

intensity of absorption. The specificity of the absorption of the biuret complexes, which, first of all is characterized by the position of the maximum and by the comparative intensity of absorption in various parts of the spectrum, must depend exclusively on the character of the coordination bonds between the copper atom and the groups capable of coordination compound formation. The following structures were considered possible for the coordination compound studied. The structure of the diglycylglycine coordination compound previously given is shown here for comparison.

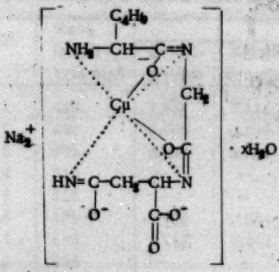


Diglycylglycine coordination compound



Alanylglycylglycine coordination compound

The fact that the appearance of a fourth nitrogen atom in the tripeptide leucylglycylasparagine (as compared to diglycylglycine) leads to the formation of a "red" coordination compound, instead of the "violet" characteristic of tripeptides, is considered to be of great importance.



Leucylglycyl-asparagine coordination compound

Of the three possible structural formulas for the leucylglycyltryptophan complex, the most probable is (III). If structure (I) was correct, then the absorption maximum would be shifted towards the shorter wavelengths and the color of the coordination compound would be red. According to structure (II), the nitrogen atom of the indole ring does not take any part in the coordination compound formation; according to this, the character of the absorption of the leucylglycyltryptophan coordination compound should be the same as for the diglycylglycine complex, differing only in the intensity of the absorption. Structure (II) cannot explain the 7 mμ shift toward the longer wavelength that is found for the leucylglycyltryptophan coordination compound.

Structure (III) provides for a saltlike link between the copper atom and the nitrogen atom of the indole ring. Of course supplementary experiments will be necessary to see if this linkage can be formed under the conditions of the biuret reaction.

Iodometric determination of copper in the glycylglycylthreonine coordination compound shows that there is more than one mole of the peptide for each atom of copper. It is possible that the iodometric method for the determination of copper gives lower figures in the presence of the tripeptide, glycylglycylthreonine. It is still difficult to propose a structure other than the one pictured above. Undoubtedly the cause of the very significant change in the character of the absorption spectrum when threonine is introduced into the tripeptide is due to the hydroxyl group taking part in the coordination compound formation.

2. Dipeptide copper biuret complexes

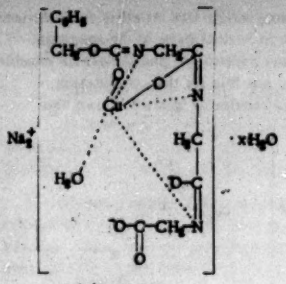
The results of the iodometric determination of the copper in dipeptide complexes are given in Table 3.

The amount of copper in all of the dipeptide complexes is somewhat low. Apparently the lack of reactivity for the formation of complexes is a general property of the dipeptides.

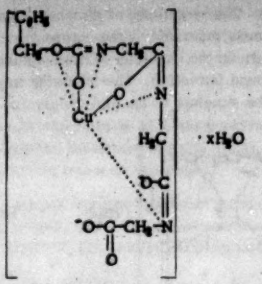
The spectrophotometric study of the dipeptide complexes led to the results given in Table 4 and Fig. 2.

The following conclusions were drawn from the results:

1. The absorption maximum of the glycylasparagine coordination compound lies at 532.2 mμ. The introduction of asparagine into the dipeptide sharply shifts the absorption maximum toward the shorter wavelengths (analogous results were obtained for the tripeptide leucylglycylasparagine).

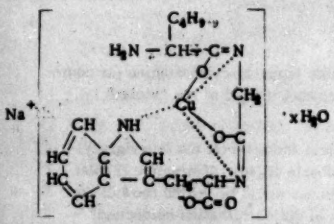


Schema (I)

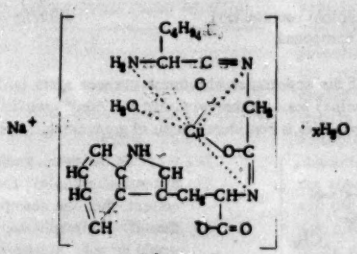


Schema (II)

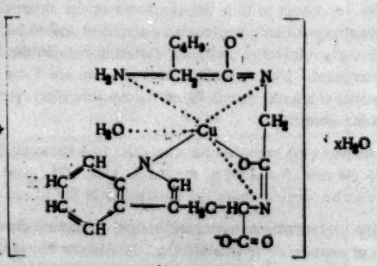
Carbobenzoxydiglycylglycine coordination compound.



Schema (I)

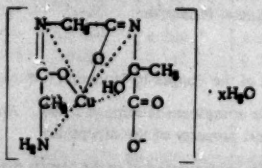


Schema (II)



Schema (III)

Leucylglycyltryptophan coordination compound



Glycylglycylthreonine coordination compound.

2. The absorption maximum of the glycylthreonine coordination compound lies at 645 mμ. The introduction of threonine into the dipeptide noticeably shifts the absorption maximum of the coordination compound toward the shorter wavelengths. (Analogous results were obtained for the tripeptide glycylglycylthreonine).

TABLE 3

Amount of copper in the dipeptide biuret coordination compounds

No.	Dipeptide	Amount of copper per mole of peptide	
		(in g)	(in moles)
1	Glycylthreonine	50.4	0.80:1
2	Glycylasparagine	53.6	0.84:1
3	Leucylhistidine	25.08	0.39:1
4	Glycyltyrosine	64.7	1.17:1
5	Glycylglycine	54.0	0.85:1

3. The absorption maximum of the glycyltyrosine coordination compound lies at 630 mμ. The introduction of tyrosine into the dipeptide shifts the absorption maximum of the coordination compound toward the shorter wavelengths.

4. The absorption maximum of the glycyltryptophan coordination compound lies at 630 mμ. The introduction of tryptophan shifts the absorption maximum of the coordination compound toward the shorter wavelengths. In this case a different phenomenon from that found for the tripeptide leucylglycyltryptophan is observed.

5. The absorption maximum of the carbobenzoxyglycylglycine coordination compound lies at 620 mμ. The replacement of one of the hydrogen atoms on the amino group leads to the shift of the absorption maximum of the coordination compound toward the shorter wavelengths.

Therefore an analogy is found in the behavior of the dipeptides and tripeptides, in the sense that the presence of different amino acids in the peptides leads to differences in the character of the absorption of the coordination compound. It is very interesting that the amino acid which causes the greatest shift in the absorption maximum of the tripeptide coordination compound has the greatest influence on the character of the absorption of the dipeptide coordination compound. For example, the introduction of asparagine into the tripeptide as well as the dipeptide causes an extremely sharp shift of the absorption maximum of the coordination compound. The absolute magnitude of the shift is not the same, as expected, as the structure of the dipeptide has its own peculiarities. Previously it had been considered that two molecules of the peptide and one copper atom form the coordination compound with glycylglycine. More correct determinations of copper and certain properties of this coordination compound have now led to the conclusion that the ratio is 1:1. Moreover, the dipeptide biuret coordination compound appears to be an incompletely formed coordination compound, and its activity of formation is considerably lower than for

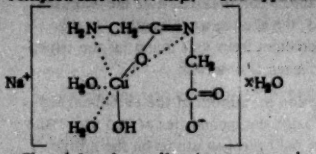
TABLE 4

Optical density of the dipeptide copper-biuret coordination compounds and their derivatives

No.	Wave length λ(in mμ)	Magnitude of the optical density, ε						
		Glycyl-glycine	Glycyl-threonine	Glycylas-paragine	Glycyl-tryptophan	Leucyl-histidine	Glycyl-tyrosine	Carbobenzoxy-glycylglycine
1	480	0.054	0.116	0.272	0.028	0.099	0.092	0.036
2	490	0.066	0.135	0.297	0.033	0.112	0.113	0.046
3	505	0.078	0.186	0.351	0.038	0.133	0.142	0.066
4	510	—	—	—	—	—	0.160	—
5	515	—	—	—	—	—	—	—
6	520	0.093	0.224	0.396	0.045	0.153	0.184	0.087
7	530	0.108	0.249	0.423	0.051	0.163	0.211	0.102
8	535	—	—	0.423	—	—	—	—
9	540	0.108	0.289	—	0.057	0.173	0.240	0.121
10	550	0.132	0.316	0.413	0.064	0.182	0.276	0.141
11	560	0.149	0.346	0.396	0.070	0.187	0.314	0.161
12	570	0.167	0.373	0.383	0.078	0.188	0.355	0.180
13	575	—	—	—	—	0.188	—	—
14	582	0.192	0.400	0.353	0.088	0.186	0.401	0.201
15	600	0.228	0.435	0.292	0.098	0.170	0.465	0.225
16	610	0.251	0.442	0.266	0.102	0.158	0.441	0.228
17	615	—	0.449	—	—	—	—	—
18	620	0.278	0.441	0.233	0.105	0.141	0.505	0.229
19	625	—	—	—	—	—	—	0.228
20	630	0.301	0.429	0.204	0.107	0.134	0.512	0.228
21	635	—	—	—	—	—	0.510	—
22	640	0.322	0.409	0.176	0.105	0.122	0.505	0.224
23	650	0.352	0.396	0.153	0.104	0.110	0.495	0.211
24	670	0.395	0.334	0.112	0.094	0.083	0.450	0.175
25	693	0.385	0.254	0.076	0.078	0.064	0.377	0.130
26	710	0.349	0.200	0.058	0.068	0.052	0.319	0.101
27	730	0.271	0.143	0.010	0.054	0.039	0.252	0.072

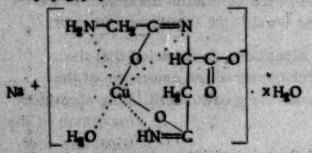
the tripeptide and somewhat higher than for the tetrapeptide. The blue color of the glycylglycine coordination compound and, in particular, the absorption of this coordination compound in the visible part of the spectrum, should be explained by the structure given below.

The incomplete nature of the glycylglycine coordination compound is explained only by the fact that the two coordinate valences are saturated by bonds with two molecules of water because of incomplete salt formation. One of the principal valences of copper remains bound with the hydroxyl. The absorption maximum of this complex lies at 670 mμ. The appearance of an amino acid containing a supplementary functional group in the dipeptide leads to a shift in the absorption maximum. It follows that one or the other of the bonds existing in the glycylglycine coordination compound are changed to bonds which are able to absorb at shorter wave lengths.

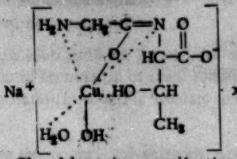


Glycylglycyl coordination compound

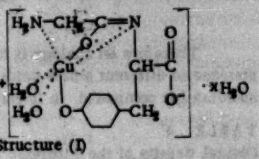
Of the two possible structures for the glycyltyrosine coordination compound the most probable appears to be (I), where a salt-forming bond exists between the copper atom and the phenolic hydroxyl.



Glycylasparagine coordination compound

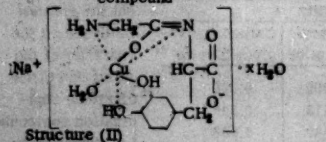


Glycylthreonine coordination compound



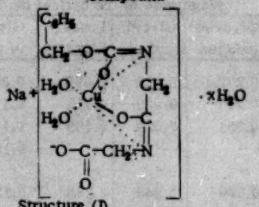
Structure (I)

Glycyltyrosine coordination compound

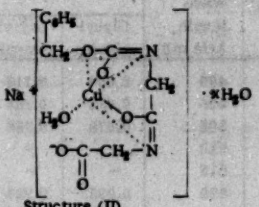


Structure (II)

Glycyl-tyrosine coordination compound

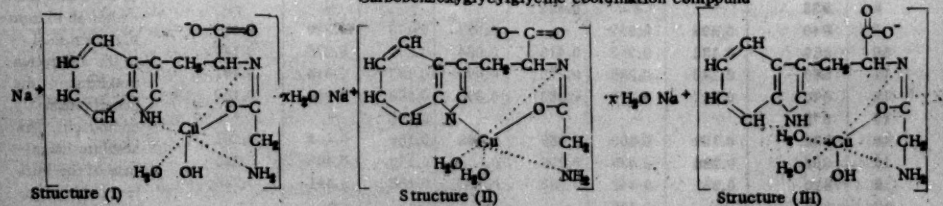


Structure (I)



Structure (II)

Carbobenzoxyglycylglycine coordination compound



Structure (I) Structure (II) Structure (III)

Glycyltryptophan coordination compound

Of the three possible structures for the glycyltryptophan coordination compound the most probable appears to be Structure (II). Structure (I) is less probable because the shift of the maximum in this case would be much greater, the coordination compound would have belonged to the "violet" group. According to Structure (III), the indole ring does not take part in the coordination compound formation, which gives no explanation for the change in the character of the absorption.

Reviewing the results obtained, it can be stated that in all cases (with one exception), the change of glycine in the tripeptide diglycylglycine and the dipeptide glycylglycine to an amino acid with some sort of supplementary functional group leads to the shift of the absorption to the shorter wavelength region.

The tripeptide containing asparagine forms the "red" coordination compound that containing threonine, the "red violet".

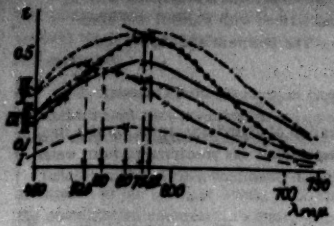


Fig. 1. Spectrophotometric curves of the tripeptide copperbiuret coordination compounds (1/150 molar solutions).

I) Carbobenzoxydiglycylglycine; II) alanylglycylglycine; III) diglycylglycine; IV) glycylglycylthreonine; V) leucylglycylasparagine; VI) leucylglycyltryptophan.

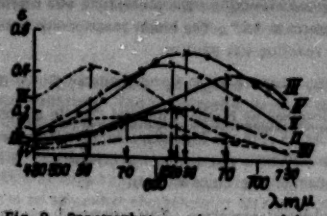


Fig. 2. Spectrophotometric curves of the dipeptide copper-biuret coordination compounds.

I) Glycyltryptophan; II) carbobenzoxyglycylglycine; III) glycylglycine; IV) glycyltyrosine; V) glycylthreonine; VI) glycylasparagine; VII) leucylhistidine

The tripeptide chain in the protein molecule consists of many different amino acids, and for this reason the character of the absorption of the coordination compounds differs somewhat for different proteins. The shift of the absorption maximum toward the shorter wavelengths which is found with the protein coordination compounds as compared to the diglycylglycine coordination compounds can be best explained by the presence of various amino acids that form the peptide chain of the protein molecule.

EXPERIMENTAL

I. Synthesis of the Peptides.

1. Preparation of glycylthreonine. This compound was not reported in the literature. A method, based on that of Fischer and Rosner [6] for the synthesis of glycylserine, was used. Glycylthreonine was synthesized by reacting chloroacetyl chloride with the sodium salt of threonine, followed by the treatment of the chloroderivative with ammonia.

$$ClCH_2COCl + H_2NCHCOONa \longrightarrow ClCH_2CONHCHCOONa \longrightarrow H_2NCH_2CONHCHCOOH$$
$$\qquad\qquad\qquad\quad CHOH \qquad\qquad\qquad\quad CHOH \qquad\qquad\qquad\quad CHOH$$
$$\qquad\qquad\qquad\quad CH_3 \qquad\qquad\qquad\quad CH_3 \qquad\qquad\qquad\quad CH_3$$

2.1 ml of chloroacetyl chloride and 18 ml of 1N NaOH were added alternately in three portions over a 30 minute period to a solution of 1.5 g of threonine in 14.4 ml of 1N NaOH, well cooled with ice and salt. At the end of the addition, the stirring was continued for 30 minutes, after which time the solution was acidified with 14.4 ml of 1 N HCl. The clear colorless solution was left to stand for 1 hour. It was evaporated to dryness in vacuum. Toward the end, small portions of alcohol were added. The residue was treated three times with hot methyl acetate. The ester was distilled and an almost colorless oil remained. The oil was treated with 10 ml of 25 % aqueous ammonia for two days in the cold. The ammonia was vacuum distilled. The residue was dissolved in a small amount of water and precipitated with alcohol. The white precipitate was filtered, washed with alcohol and ether, and dried in a vacuum desiccator. It gave a violet-blue biuret reaction. The ninhydrin reaction was positive. A negative reaction for chlorine was given.

Found %: Total nitrogen 12.57. $C_6H_{12}O_4N_2 + 2H_2O$. Calculated %: N 12.39.

2. Preparation of glycylglycylthreonine. The compound was not reported in the literature.

$$ClCH_2COCl + H_2NCH_2CONHCHCOOH \longrightarrow ClCH_2CONHCH_2CONHCHCOOH \longrightarrow H_2NCH_2CONHCH_2CONHCHCOOH$$
$$\qquad\qquad\qquad\quad CHOH \qquad\qquad\qquad\qquad\quad CHOH \qquad\qquad\qquad\qquad\quad CHOH$$
$$\qquad\qquad\qquad\quad CH_3 \qquad\qquad\qquad\qquad\quad CH_3 \qquad\qquad\qquad\qquad\quad CH_3$$

0.6 ml of chloroacetyl chloride and 3.8 ml of 1 N NaOH were added alternately in 3 portions, over a 30 minute period, to a solution of 1 g of glycylthreonine in 6 ml of 1 N NaOH. The stirring was continued for 30 minutes or more. The solution was acidified with 7 ml of 1 N HCl. After an hour, it was evaporated to dryness. It was extracted with hot methyl acetate and the solution dried with Na_2SO_4 overnight, and the ether distilled:

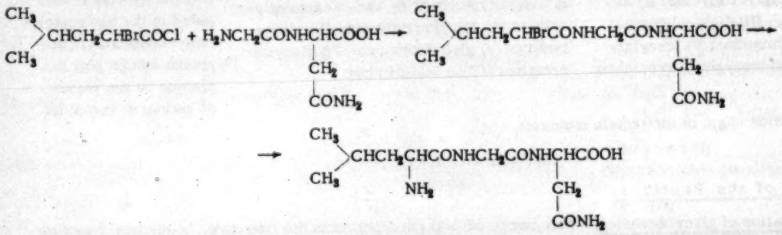
a light colorless oil remained. The oil was treated with 10 ml of 25% aqueous ammonia for two days in the cold. The ammonia was vacuum distilled, the residue dissolved in a small quantity of water, and precipitated with alcohol. A white precipitate formed overnight. The precipitate was filtered and washed with alcohol and ether. It was dried in a vacuum desiccator at 100°. The biuret reaction was positive. The Beilstein and $AgNO_3$ tests were negative. The ninhydrin reaction was positive.

Found %: Total nitrogen 18.12. $C_6H_{15}O_3N_3$. Calculated %: N 18.08.

3. Glycylasparagine, obtained by Fischer's method [7]. In the preparation of glycylasparagine, in the final stage it was found difficult to obtain it in the crystalline form. When glycylasparagine was precipitated from water with alcohol, it came out as an oil which was difficult to crystallize. A manifold treatment with absolute alcohol, however, resulted in the formation of fine white crystals.

4. Preparation of leucylglycylasparagine. This compound was not reported in the literature. Fischer's synthesis of leucylglycine-1-asparaginic acid was employed for the preparation.

The reaction went according to the equation:



0.8 ml of bromoisocaproyl chloride and 2.8 ml of 1 N NaOH were added alternately, in three portions in one hour to a solution of 0.8 g of glycylasparagine in 4.5 ml of 1 N NaOH well cooled with ice and salt. It was acidified with 1.5 ml of 5 N HCl. A clear oil came out. The water was vacuum distilled. The residue, an oil, was dissolved in a small amount of ethyl alcohol and treated with 10 ml of a 25% aqueous solution of ammonia for two days. The ammonia was vacuum distilled. The residue was processed several times with boiling absolute alcohol. Finally, it was filtered rapidly, washed with absolute ether, and transferred to a vacuum desiccator, where it was dried over calcium chloride, and subsequently for 1 hour in the vacuum desiccator at 100°. Yield 27% of theory.

The substance gave a red-violet reaction. The ninhydrin reaction was positive.

Found %: Total nitrogen 17.43. $C_{12}H_{22}O_5N_4 + H_2O$. Calculated %: N 17.49.

5. Synthesis of glycyltryptophan and leucylglycyltryptophan was accomplished by the method of Abderhalden and Kempe [8].

6. Synthesis of glycyltyrosine and alanylglycylglycine was effected by Fischer's method [9].

II. The Spectrophotometry of the Biuret Coordination Compounds

Solutions of the biuret complexes were prepared in the following manner: A sample of the peptide calculated to a 1/150 molar concentration, was dissolved in 7 ml of water, 2 ml of NaOH, and 1 ml of 1/4 molar copper acetate. After one hour, the trace of copper hydroxide was filtered off. The solution was examined spectrophotometrically on a Beckman instrument.

The amount of copper in the biuret coordination compound solution was determined iodometrically.

SUMMARY

1. The change of one of the glycines in the tripeptide diglycylglycine to amino acid containing a supplementary functional group leads to the shift in the absorption maximum of the copper-biuret coordination compound toward the shorter wavelengths. The influence of the amino acid varies. An extremely large shift occurs with the appearance of asparagine in the tripeptide.

2. The change of one of the glycines in the dipeptide glycylglycine to amino acid with a supplementary functional group leads to a shift in the absorption maximum of the biuret coordination compound (to a varied degree) toward the shorter wavelengths. An extremely strong effect is felt with the appearance of asparagine in the dipeptide.

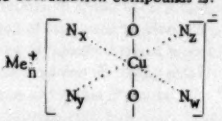
3. Oxygen containing groups (for example the hydroxy group of tyrosine and threonine) in the di- and tripeptides take part in coordination compound formation. The coordination bonds of the oxygen-containing groups absorb at longer wavelengths than the coordination bonds of nitrogen-containing groups.

4. The absorption of light of the biuret complex appears to be somewhat of an additive effect of the absorption of the separate bonds. The absorption of light by the coordinate bonds formed by the various groups – the coordination compound formers – appears to be somewhat characteristic for each bond. The position of the absorption maximum of the biuret complex depends on the coordination bonds; the intensity of absorption on the molecular weight.

5. This combined ability to absorb light is suggested as a basis for the classification of the biuret coordination compounds. The coordination compounds may so be separated into three main groups:

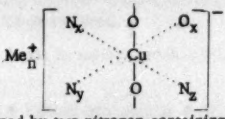
I. "Perfect" reds – formed with four nitrogen-containing groups; the absorption maximum of the coordination compound is at 515-535 mμ.

The general structure of these coordination compounds is:



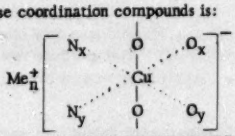
II. "Imperfect" violets – formed by three nitrogen-containing groups and one oxygen-containing group. The absorption maximum of the coordination compound is at 540-580 mμ.

The general structure of these coordination compounds is:



III. "Imperfect" blues – formed by two nitrogen-containing groups and two oxygen-containing groups. The absorption maximum of the coordination compounds is at 615-670 mμ.

The general structure of these coordination compounds is:



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*See Consultants Bureau translation, p. 2181.

**See Consultants Bureau translation, p. 341, 347, 635, 641.

SOME REACTIONS OF CYANOETHYLATION PRODUCTS OF DIHYDRIC PHENOLS WITH ACRYLIC ACID NITRILE

B. A. Arbuzov and Z. G. Isaeva

Cyanoethylation by means of acrylic acid nitrile acting upon compounds containing active hydrogen, in the presence of alkaline catalysts, has been widespread. A complete review of the literature of cyanoethylation has been given by Bruson [1].

Phenols react with acrylic acid nitrile in the presence of sodium, giving the corresponding cyanoethyl ethers [1]. As to dihydric phenols, there are patent facts that pyrocatechol and hydroquinone cyanoethylate in the presence of 1% sodium at 120-140°, giving mono- or di-cyanoethyl ethers, depending upon the amount of acrylic acid nitrile [2]. Resorcinol, according to the data of Langley and Adams [3], condenses with acrylic acid nitrile in the presence of hydrogen chloride and of zinc chloride, giving the lactone of β-(2,4-dihydroxyphenyl)-propionic acid. Cook and Reed [4] cyanoethylated pyrocatechol, resorcinol, and hydroquinone in the presence of sodium methylate, and obtained corresponding di-β-cyanoethoxybenzenes. Bachman and Levine found [5] that resorcinol in the presence of "Triton B" gives, 1,3-bis(β-cyanoethoxy)-benzene in 40% yield.

Knowledge of cyanoethylation of dihydric phenols is confined to these data.

The authors cyanoethylated pyrocatechol, resorcinol and hydroquinone in order to study certain transformation products of cyanoethylation. The yields and boiling points of the dicyano ethers obtained correspond to the data of Cook and Reed, excluding 1,4-di-β-cyanoethoxybenzene, for which the authors obtained a 70% yield, instead of 50% as indicated by Cook and Reed.

In the present article are cited data on saponification, alcoholation, and certain cyclization reactions of the obtained dinitriles.

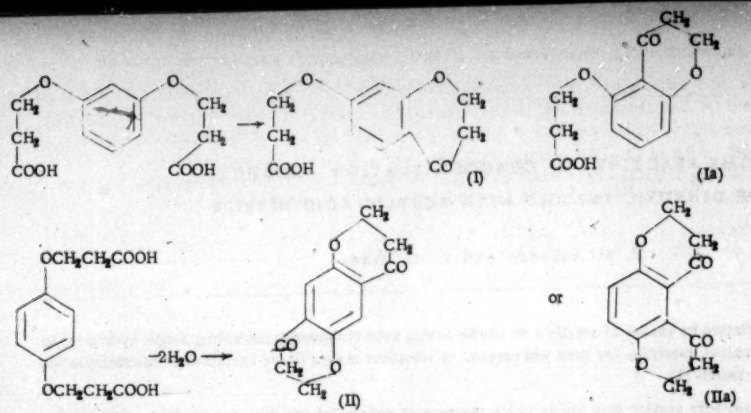
Saponfication of nitriles by 35% hydrochloric acid gave the corresponding dibasic acids. 1,2-Di-β-carboxyethoxybenzene had an m.p. of 155-157°, 1,3-di-β-carboxyethoxybenzene, m.p. 173-175°, and 1,4-di-β-carboxyethoxybenzene, m.p. 197-199°. 1,3-Di-β-cyanoethoxybenzene, by the action of alcohol in the presence of hydrogen chloride, was converted into the diethyl ester, b.p. 195-197° at 4.5 mm and m.p. 39-40°, which, upon saponification, gave the same acid with m.p. 173-175°. By the action of thionyl chloride on the obtained acids, corresponding full chloranhydrides were obtained. The chloranhydride of 1,3-di-β-carboxyethoxybenzene had an m.p. of 71-74°. In the case of 1,4-di-β-carboxyethoxybenzene, the full chloranhydride resulted, m.p. 91-93°.

The authors also conducted some cyclization experiments on the obtained free acids of 1,3- and 1,4-derivatives of benzene. Bachman and Levine [5] carried out cyclization of 1,3-di-β-cyanoethoxybenzene with 85% sulfuric acid, and obtained a product in 12.8% yield, m.p. 171-173°, to which they gave the structure 7-β-carboxyethoxychromanone [1]. The authors conducted cyclization reactions of 1,3-di-β-carboxyethoxybenzene by heating it with phosphoric anhydride, phosphoric acid being present. This gave a product with an m.p. identical to the product of Bachman and Levine, but in considerably greater yield (43.6%). The validity of its structure (Ia) was not studied.

The cyclization product contains one free carboxyl group, and upon reaction with semicarbazide hydrochloride gave a semicarbazone, m.p. 219-220°, which the authors were not able to obtain in an analytically-pure state.

Upon heating 1,3-di-β-carboxyethoxybenzene with phosphoric anhydride in phosphoric acid, a crystalline product was obtained, m.p. 229-230°, 23.2% yield, corresponding to the diketone.

The structure, in the sense of choice between (II) and (IIa), was not determined by the authors.



EXPERIMENTAL

Saponification of 1,2-di-β-carboxyethoxybenzene by hydrochloric acid. Taken for reaction were 1.4 g of 1,2-di-β-cyanoethoxybenzene, m.p. 118-120° and 20 ml of 35% hydrochloric acid. The mixture was heated on a water bath until the 1,2-di-β-cyanoethoxybenzene dissolved. Upon cooling of the reaction mixture, crystals separated, which were filtered off, washed with water and dried. Weight 0.53 g (32.6% yield) m.p. 155-157°. Recrystallization from alcohol did not change the m.p.

0.0926 g substance: 0.1700 g CO_2; 0.0518 g H_2O. 0.1044 g substance: 0.2016 g CO_2; 0.0564 g H_2O. Found %: C 52.72, 52.66; H 6.21. 6.00. $C_{12}H_{12}O_6$. Calculated %: C 56.69; H 5.51. $C_{12}H_{14}O_6 \cdot H_2O$. Calculated %: 52.94; H 5.88.

Saponification of 1,3-di-β-cyanoethoxybenzene by hydrochloric acid. Taken for reaction were 5 g of 1,3-di-β-cyanoethoxybenzene, m.p. 110-111°, and 25 ml of hydrochloric acid. The mixture was heated at 60-65° for 8.5 hours. The product was filtered, washed with water and dried, m.p. 172-175°. After a double recrystallization the product melted at 173-175°. Weight 3.9 g (yield 66.4%).

0.0980 g substance: 0.2028 g CO_2; 0.0514 g H_2O. Found %: C 56.49. H 5.82. $C_{12}H_{14}O_6$. Calculated %: C 56.69; H 5.51.

Alcoholysis of 1,3-di-β-cyanoethoxybenzene. 5 g of 1,3-di-β-cyanoethoxybenzene was dissolved in 150 ml of absolute ethanol. Dry hydrogen chloride was passed through the solution heated to boiling for 14 hours. The precipitated ammonium chloride sediment was filtered off. The filtrate was poured into water and extracted with ether. The ether extract was dried with calcium chloride. The ether was distilled off, and the residue distilled in vacuo. Obtained was 1.8 g of product, b.p. 195-197° at 4.5 mm, yield 19.7%. On standing, the product crystallized, m.p. 39-40°.

0.1206 g substance: 0.2727 g CO_2; 0.0786 g H_2O. Found %: C 61.67; H 7.24. $C_{16}H_{22}O_6$. Calculated %: C 61.90; H 7.15.

Saponification of the ethyl ether of 1,3-di-β-carboxyethoxybenzene. 0.3 g of the ether and 5 ml of 35% hydrochloric acid were heated on a water bath at 40-50° for 30 minutes. Upon cooling a precipitate settled out, which was filtered, washed with water and dried. After two recrystallizations from ethanol, 0.25 g of substance was obtained, m.p. 172-174°. The sample was mixed with 1,3-di-β-carboxyethoxybenzene, obtained by saponification of 1,3-di-β-cyanoethoxybenzene, and the mixture melted at 172-174°.

Reaction of thionyl chloride with 1,3-di-β-carboxyethoxybenzene. 3.5 g of 1,3-di-β-carboxyethoxybenzene and 15 ml of dry benzene in 16.2 g thionyl chloride were taken for reaction. The mixture was carefully heated upon a water bath until the 1,3-di-β-carboxyethoxybenzene dissolved. After distilling off the benzene and thionyl chloride in vacuo, there remained in the flask a pasty mass which partially crystallized. The chloranhydride was extracted with gasoline by warming. Crystals separated from the extract in very small quantity, which, after two recrystallizations from cyclohexane, melted at 71-74°.

0.0444 g substance; 0.0436 g HgCl. Found %: Cl 24.30. $C_{12}H_{12}O_4Cl_2$. Calculated %: Cl 24.39.

Cyclization of 1,3-di-β-carboxyethoxybenzene. Taken for reaction were 4.8 g of product, 50 g of phosphoric anhydride and 100 g of phosphoric acid (1.75). 6.6 times the theoretical weight of phosphoric anhydride necessary for splitting out two molecules of water from the dibasic acid was used. The mixture was heated 4 hours on a water bath. After cooling, the mixture was poured into cold water. The precipitate was filtered off, washed with water and recrystallized from alcohol. 1.9 g of substance, m.p. 169-171, was obtained. Yield of monoketone, 46.3%.

0.0994 g substance: 0.2224 g CO_2; 0.0754 g H_2O. Found %: C 61.02; H 5.20. $C_{12}H_{12}O_5$. (monoketone). Calculated %: C 61.01; H 5.12.

The product with an m.p. of 169-171 was titrated with NaOH solution (NaOH = 0.01928N): 0.0414 g of substance dissolved in 34 ml redistilled alcohol required 0.6 ml of the NaOH solution. Blank test – for 34 ml alcohol, 0.25 ml NaOH solution: given weight of substance required 0.85 ml NaOH solution.

Found: 0.006748 g NaOH. $C_{12}H_{12}O_5$. Calculated: 0.00701 g NaOH.

1,4-Di-β-cyanoethoxybenzene saponification by hydrochloric acid. 5.2 g of the condensation product of hydroquinone with acrylic acid nitrile was saponified by 35% hydrochloric acid by heating on a water bath for 10 hours. After two recrystallizations from acetic acid 5.2 g of substance, m.p. 197-199°, was obtained, yield 85.2%.

0.0932 g substance: 0.1932 g CO_2; 0.0498 g H_2O. Found %: C 56.53; H 5.93. $C_{12}H_{14}O_6$. Calculated %: C 56.69; H 5.51.

Reaction of thionyl chloride with 1,4-di-β-carboxyethoxybenzene. Taken for reaction were 5.2 g of 1,4-di-β-carboxyethoxybenzene and 24.4 g (14.5 ml) of thionyl chloride. The mixture was heated until the 1,4-di-β-carboxyethoxybenzene dissolved. The excess thionyl chloride was distilled off at atmospheric pressure, traces – in vacuo. The residue was extracted with gasoline. 4.7 g of crystalline product was obtained, m.p. 91-93°, yield 60%.

0.1072 g substance: 0.1047 g AgCl. 0.1254 g substance: 0.1227 g AgCl. Found %: Cl 24.19, 24.25. $C_{12}H_{12}O_4Cl_2$. Calculated %: Cl 24.39.

Cyclization of 1,4-di-β-carboxyethoxybenzene. Taken for reaction were 5 g of di-β-carboxyethoxybenzene, 50 g of phosphoric anhydride, and 100 g of phosphoric acid (s.g. 1.75). The mixture was heated on a water bath for 10 hours. After cooling, the mixture was poured into water and the yellow precipitate filtered off, washed with water, and dried. After one recrystallization from benzene its m.p. was 227-229°; after a second recrystallization its m.p. was 229-230°. Yield 23.2%.

0.0832 g substance: 0.2002 g CO_2; 0.0336 g H_2O. Found %: C 65.62; H 4.48. $C_{12}H_{10}O_4$. Calculated %: C 66.05; H 4.58.

SUMMARY

1. By saponification of 1,2-di-β-cyanoethoxybenzene, 1,3-di-β-cyanoethoxybenzene and 1,4-di-β-cyanoethoxybenzene the corresponding acids were obtained. The full chloranhydrides of 1,3-di-β-carboxyethoxybenzene, 1,4-di-β-carboxyethoxybenzene, and the ethyl ester of 1,3-di-β-carboxyethoxybenzene were obtained.

2. 1,3-Di-β-carboxyethoxybenzene cyclization by phosphoric anhydride was carried out in phosphoric acid medium. A product identical with that of Bachman and Levine was obtained. 1,4-Di-β-carboxyethoxy benzene cyclization by phosphoric anhydride in phosphoric acid medium gives double ring closure.

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SYNTHESIS AND STUDY OF γ-DIETHYLAMINOPROPYL ETHER OF 2-METHOXY-6-ALLYLPHENOL

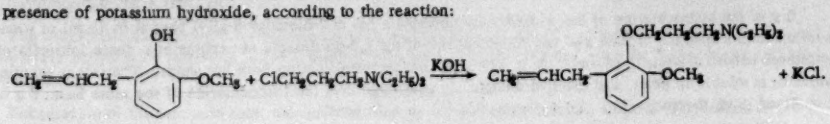
A. M. Khaletsky and T. I. Sokolova

By a series of examples of aromatic compounds with molecules having an unsaturated alkyl radical in the position ortho to phenylhydroxyl, etherified by an alkylamino group, as for example: β-dimethylaminoethyl ether of 2-methoxy-6-allylphenol, β-diethylaminoethyl ether of 2-methoxy-4,6-diallylphenol, β-diethylaminoethylether of 2-methoxy-6-crotylphenol, and β-diethylaminoethyl ether of 1-allylnaphthol – it was shown that such compounds are endowed with hemostatic and uterine activity [1]. Among these compounds the most interesting appeared to be the β-diethylaminoethyl ether of 2-methoxy-6-allylphenol [3], which, under the name of pregnantol or gravitol, in the hydrochloride or citrate form, has found application in medical practice as a replacement for galenic preparations of ergot [2]. It follows therefore, it should be noted, that among the uterine remedies there predominate mostly preparations of vegetative origin (ergot, shepherd purse, snowball tree, water, pepper and others); synthetic preparations, excluding pregnantol, being practically represented by only stiptisin and hydrostinin, obtained by oxidation of narcotin or of hydrostin. The unavailability of hydrostin, and thus the impossibility of obtaining hydrostinin, further reduces the number of synthetic uterine and hemostatic remedies.

The presence, in the pregnantol molecule, of a free radical and alkyl amino group makes it interesting to study this class of compounds for the purpose of demonstrating the relation between their chemical structure and activity. Since the effect of the alkylamino group upon pharmacological activity has been repeatedly on a series of examples (anesthetic p.H., derivatives of acridine [5], and others) one can assume that the physiological action of pregnantol is tied up with this group. To study this dependence we synthesized the nearest analog to pregnantol – the γ-diethylaminopropyl ether of 2-methoxy-6-allylphenol.

By interaction of guaiacol and allyl bromide in the presence of potassium, there was obtained the allyl ether of guaiacol [6] which, upon heating to 240°, isomerized to 6-allylguaiacol [7]. The ease with which the allyl radical passes over from oxygen to carbon [8] was utilized in the present case.

The 6-allylguaiacol synthesized by the authors was reacted further with diethylaminopropyl chloride in the presence of potassium hydroxide, according to the reaction:



Pharmacological tests of the hydrochloride salt and the salt obtained by interaction of the hydrochloride base with the potassium salt of the 1,5-disulfo acid of naphthalene, which were carried out by the Department of Pharmacology of the author's Institute, have less effective uterine action compared with the β-diethyl aminoethyl ether of 2-methoxy-6-allylphenol, which follows because of the lengthening of the alkylamino group chain by a $-CH_2-$.

EXPERIMENTAL

2-Methoxy-6-allylphenol. 120 g of allyl ether guaiacol, obtained by the method of Claison [6], underwent isomerization by heating to 240° for 2 hours, the reaction product being then treated with 60 ml of 5% solution of sodium hydroxide in the presence of 50 ml of ether. The colorless alkaline liquid was neutralized by dilute hydrochloric acid; the precipitated 6-allylguaiacol extracted with ether; the ether liquid washed with water and dried over potassium oxide, and after removal of the ether, fractionated; 80 g of 2-methoxy-6-allylphenol

was obtained, b.p. 120° at 12 mm (96% of the theoretical). For identification of 2-methoxy-6-allylphenol, its allyl ether was synthesized and isomerization to 2-methoxy-6-propylphenol carried out.

16.4 g of 2-methoxy-6-allylphenol was heated with 12.5 g of allyl bromide and 12 g of potash in acetone medium (50 ml) for 6 hours on a water bath. After cooling, water was added to the reaction mixture to dissolve the salts, and the solution obtained was washed with ether after drying of the ether solution by sodium sulfate, then followed by distillation of the ether, the residue, distilled at 130-131°, under 12 mm pressure, yield 16 g (78% of theoretical).

Isomerization of 2-methoxy-6-allylphenol into 2-methoxy-6-propenylphenol was effected by heating 5 g of 2-methoxy-6-allylphenol with 10 g of solid potassium hydroxide in 5 g of water to 170° for 1 hour. The resulting cake was dissolved in water, acidified with hydrochloric acid and washed with ether; the ether solution was dried over anhydrous sodium sulfate, and the ether distilled off. The small amount of residue recovered (2 - 2.5 g) soon crystallized; recrystallized from hot benzene, the substance appeared as long, shiny needles with the odor of oil of cloves, m.p. 76°, corresponding to o-isoeugenole.

γ-Diethylaminopropyl ether of 2-methoxy-6-allylphenol. 44 g of 2-methoxy-6-allylphenol was dissolved in 130 g of 10% potassium hydroxide, and 50 g of 1-diethylamino-3-chloropropane (25% excess) was gradually added, upon which warming up (from 15 to 32°) was observed; subsequently the mixture was heated to boiling on an oil bath at 140-160° for 8 hours. The separated oily layer was extracted with ether. The ether solution was washed with a solution of potassium hydroxide, with water, and then dried over calcium chloride. After removal of the ether, the residue was fractionated; there separated a fraction with b.p. 178-181° at 8 mm pressure in the amount of 55 g (76% theoretical), in the form of a colorless, transparent liquid, insoluble in water, soluble in alcohol, ether, chloroform, benzene, and mineral acids.

0.1495 g substance: 0.4035 g CO_2; 0.1348 g H_2O. 0.1567 g substance: 0.4220 g CO_2; 0.1401 g H_2O. 0.2762 g substance: 10.29 ml 0.1 N. HCl (Kjeldahl). 0.2607 g substance: 9.59 ml 0.1 N. HCl. 0.4231 g substance: 15.30 ml 0.1 N. HCl. 0.3572 g substance: 12.90 ml 0.1 N. HCl. Found %: C 73.61, 73.45; H 10.00, 10.09; N 5.22, 5.15; M 276.6, 276.9. Calculated %: C 73.60; H 9.82; N 5.05; M 277.2. 1.93 mg substance; 4.58 mg camphor: Δt 7° (Rast). Found: M 299.6.

Hydrochloride of γ-diethylaminopropyl ether of 2-methoxy-6-allylphenol. 5 g of γ-diethylaminopropyl ether of 2-methoxy-6-allylphenol was dissolved in 50 g of dry ethyl acetate and the solution saturated with hydrogen chloride; the separated white powder was filtered off and recrystallized from hot ethyl acetate. The salt was soluble in water and alcohol, insoluble in ether and chloroform, m.p. 75-77°.

0.3420 g substance: 12.30 ml 0.1 N. NaOH. 0.3843 g substance: 13.85 ml 0.1 N. NaOH. $C_{17}H_{27}O_2N \cdot HCl$. Found salt %: 99.70, 99.83.

Production of salt from γ-diethylaminopropyl ether of 2-methoxy-6-allylphenol and the 1,5-disulfoacid of naphthalene. 1,5-Disulfoacid of naphalene, produced by sulfonation of naphthalene with 30% oleum; potassium salt separated with a 10% solution of NaCl [9].

5 g of the hydrochloride of the γ-diethylaminopropyl ether of 2-methoxy-6-allyl phenol in 50 ml of water was mixed with a solution of 2.65 g of the potassium salt of the 1,5-disulfoacid of naphthalene; there immediately precipitated needle crystals in clusters, m.p. 120-123° after recrystallization from hot water. The salt is soluble in alcohol, insoluble in ether, and non-hydroscopic, an advantage over the hydrochloride of the same base; 6 g of salt obtained (89% theoretical).

0.2698 g substance: 0.1502 g $BaSO_4$. 0.2597 g substance: 0.1459 g $BaSO_4$. Found %: S 7.65, 7.69. $(C_{17}H_{27}O_2N)_2 \cdot C_{10}H_8O_6S_2$. Calculated %: S 7.61.

SUMMARY

From 2-methoxy-6-allylphenol and 1-diethylamino-3-chloropropane was synthesized the γ-diethylaminopropyl ether of 2-methoxy-6-allylphenol as well as its hydrochloride salt with 1,5-disulfoacid of naphthalene.

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DEHYDRATION AND OXIDATION OF 2-ETHOXY-(5,6,7,8-TETRAHYDRONAPHTHOYL-3)-PROPIONIC ACID

S. I. Sergievskaya and I. M. Lipovich

Upon study of the interaction of α-2-ethoxytetrahydronaphthalene with succinic anhydride, in the presence of $AlCl_3$, S. I. Sergievskaya and A. V. Danilova [1] isolated two isomeric 2-ethoxytetrahydronaphthoylpropionic acids, and demonstrated that the keto acid group, upon condensation, enters into the 3 or the 4 position of the 2-ethoxytetrahydronaphthalene molecule; which one of the two isolated keto acids appears to be 2-ethoxy-(5,6,7,8-tetrahydronaphthoyl-3)- or 2-ethoxy-(5,6,7,8-tetrahydronaphthoyl-4)-propionic acid remained unclarified. In the present work, the authors aim to define more accurately the structure of 2-ethoxytetrahydronaphthoylpropionic acid, m.p. 169-170°, which is formed in large amount.

Upon repeating the above-mentioned reaction for the purpose of obtaining in sufficient amount the acid to be investigated, the reaction conditions and treatment of substance were changed (see Experimental Section), with the result that the keto acid yield was considerably increased, approximately three fold.

To define the structure of the ketoacid, m.p. 169-170°, we first applied the dehydration reaction with the help of 20% palladium on carbon. This method was recommended by Newman and Zahm for the analogous compounds of tetrahydronaphthalene; simultaneously with dehydration of the ring, the carbonyl group is usually reduced to the methylene group.

We proposed to obtain, with the aid of this reaction, 2-ethoxynaphthylbutyric acid, and subsequently, by means of desalkylation, to convert the ethoxyl group, thus to form hydroxynapthylbutyric acid, which could be either 2-hydroxynaphthyl-3- or 2-hydroxynaphthyl-4-butyric acid. A comparison of hydroxynaphthylbutyric acid obtained in this way with that described by G. Val [3], 2-hydroxy-3-naphthylbutyric acid, could resolve the question of the structure of the original ketoacid.

$$\left.\begin{array}{l} C_2H_5OC_{10}H_6CO(CH_2)_2COOC_2H_5 \\ C_2H_5OC_{10}H_6(CH_2)_3COOC_2H_5 \\ C_2H_5OC_{10}H_6(CH_2)_3COOC_2H_5 \end{array}\right\} \rightarrow C_2H_5OC_{10}H_6(CH_2)_3COOH \rightarrow HOC_{10}H_6(CH_2)_3COOH$$

The ethylesters of both 2-ethoxytetrahydronaphthoylpropionic acid and of 2-ethoxytetrahydronaphthylbutyric acid underwent dehydration (ethoxytetrahydronaphthylbutric acid is easily obtained from the ketoacid by a Clemmensen reaction).

Dehydration of the ketoacid ester was accompanied by marked resinification, whereas dehydration of the ester of ethoxytetrahydronaphthylbutyric acid under the same conditions proceeds with good results, and thus can be successfully utilized for obtaining exthoxynaphthylbutyric acid. The authors did not succeed in claryifying the structure of the ketoacid by the above method, because the hydroxynaphthylbutyric acid obtained after desalkylation melted at 139-141°, whereas, according to the data of G. Val, 2-hydroxynaphthyl-3-butyric acid melts at 131°. This difference in the melting points can be explained with almost equal probability by either a different degree of purity of the hydroxynaphthylbutyric acids synthesized by different methods, or by the assumption that the hydroxynaphthylbutyric acid obtained by the authors is not 2-hydroxy-3-naphthylbutyric acid, but its isomer.

The indefiniteness of the results obtained compelled the authors to make use of a second possible method for defining the ketoacid structure, namely, its oxidation to ethoxytetrahydronaphthoic acid, followed by desalkylation of the ethoxyl groups. These transformations should lead to some known hydroxytetrahydronaphthoic acids. Oxidation of 2-ethoxytetrahydronaphthoylpropionic acid with the aid of sodium hypochlorite proceeded without any special difficulty, and the same was true of the desalkylation of 2-ethoxytetrahydronaphthoic acid. As the result of these reactions, the substance obtained appeared to be hydroxytetrahydronaphthoic acid, according to the elementary

analysis data, and its melting temperature and other properties were the same as those for 2-hydroxy-3-tetrahydronaphthoic acid, as described in detail by Schroeter [4]. The melting point of the methyl ester of 2-hydroxy-3-tetrahydronaphthoic acid, obtained by the authors, also corresponded precisely with that shown for this compound by Schroeter.

On the basis of these data, the authors conclude that the ketoacid with an m.p. of 169-170° is the 2-ethoxy-(5,6,7,8-tetrahydronaphthoyl-3)-propionic acid.

EXPERIMENTAL

β-(2-Ethoxy-5,6,7,8-tetrahydronaphthoyl-3)-propionic acid $C_2H_5OC_{10}H_{10}CO(CH_2)_2COOH$. Into a vessel equipped with a mixer and reflux condenser were placed 85 g of ar-2-ethoxytetralin, 47 g of succinic anhydride, and 1120 ml of absolute nitrobenzene. Then 136 g of aluminum chloride was added in small portions, with mechanical stirring, over a period of 7 to 8 hours. The reaction proceeds at room temperature. The reaction mass was allowed to stand until the following day, when the mixing was continued for five more hours. 1200-1300 ml of water with ice and 340 ml of concentrated sodium chloride were added. A precipitate then settled out, which was filtered and washed with small portions of ether to remove nitrobenzene. 60 g of ketoacid mixture, m.p. 143-147°, was obtained. To the remaining nitrobenzene solution were added ether and a 4 % alkali solution, with shaking. The alkaline solution was separated, and the remainder of the ether removed from it by heating. The alkaline solution was filtered and acidified with 10% hydrochloric acid. The precipitated resinous sediment was sucked off and washed several times with benzene. An additional 30 g of ketone acids mixture, m.p. 130-135°, was obtained.

The isomeric mixtures of 2-ethoxy-(5,6,7,8-)tetrahydronaphthoylpropionic acids were separated according to the method of Sergievskaya and Danilova [1], by their conversion into ethyl esters. After esterification and the usual processing, the mixture of ethyl esters was separated by recrystallization from alcohol; 30 g of the ethyl ester of 2-ethoxytetrahydronaphthoylpropionic acid, m.p. 79-80°, was obtained. After saponification of this ester, 22 g of ketoacid, m.p. 169-170°, was obtained. The residue, m.p. 79-80°, after separation of the ether, was a thick mass, which contained the ethyl ester of the second isomeric acid. This residue was distilled in vacuo. 25 g of a fraction was collected at 225-228° at 4-5 mm. After saponification of this fraction 20 g of substance was obtained. After alcohol recrystallization, 10 g, m.p. 191-192° was obtained, and 10 g with m.p. 154°.

Thus, from 85 g of 2-ethoxytetralin were obtained: 22 g of ketoacid, m.p. 169-170°; 10 g of ketoacid, m.p. 191-192°; and 10 g of ketoacid mixture, m.p. 154°.

Ar-2-Hydroxytetrahydronaphthoyl-3-propionic acid. 10 g of ar-2-ethoxytetrahydronaphthoyl-3-propionic acid, m.p. 169-170°, were dissolved, by heating, in 450 ml of absolute benzene, after which the bath was set aside and 21 g of aluminum chloride added in several stages, and then heated for 5 hours. The benzene was distilled off, up to point of dryness and the residue decomposed with ice and water and 40 ml of concentrated hydrochloric acid. The precipitate was filtered off, and, upon heating, dissolved in 100 ml of 10% alkali solution, with added carbon. The alkali solution was filtered off and acidified with 10% hydrochloric acid. The separated precipitate was filtered off and washed several times with water. 7.5 g of crude substance was obtained. The substance dissolved with difficulty in hot water. After recrystallization from alcohol, the m.p. was 137-140°. Upon second recrystallization from an alcohol-benzene mixture, the m.p. was 139-142°.

For analysis, this ketoacid was further purified by converting to the ethyl ester, recrystallizing the latter, followed by saponification. Purified in this manner the ketoacid, after recrystallization from alcohol, melted at 142-144°.

4.920 mg substance: 12.311 mg CO_2; 2.879 mg H_2O. Found %: C 68.24; H 6.54. $C_{16}H_{16}O_4$. Calculated %: C 67.74; H 6.45.

Ethyl ester of 2-hydroxytetrahydronaphthoyl-3-propionic acid. To 3 g of 2-hydroxytetrahydronaphthoyl-3-propionic acid was added 30 ml of absolute alcohol and 1.7 ml conc. H_2SO_4 and the mixture was heated for 6 hours. The alcohol was distilled off, the residue diluted with water, the separated precipitate filtered off and dissolved in ether, and the ether solution washed with 3% sodium bicarbonate, then with water, and dried with anhydrous sodium sufate; the ether was distilled off and the residue distilled in vacuo. A fraction was collected with b.p. 222-223° at 5-6 mm. The substance quickly crystallized. 2.1 g, m.p. 40-42°, was obtained. After double recrystallization from alcohol, the m.p. was 43.5-45.5°.

4.322 mg substance: 11.041 mg CO_2; 2.893 mg H_2O. Found %: C 69.67; H 7.49. $C_{16}H_{20}O_4$. Calculated %: C 69.56; H 7.24.

γ-(2-Ethoxynaphthyl-3)-butyric acid. a) Dehydration of the ethyl ester of γ-(2-ethoxytetrahydronaphthyl-3)-butyric acid. The ethyl ester of γ-(2-ethoxytetrahydronaphthyl-3)-butyric acid was obtained by a Clemmensen reduction of 2-ethoxytetrahydronaphthoyl-3-propionic acid, with subsequent esterification, was obtained by this method 2-ethoxytetrahydronaphthyl-3)-butyric acid under the conditions indicated by S. I. Sergievskaya and A. V. Danilova.

To 4 g of the ethyl ester of 2-ethoxytetrahydronaphthylbutyric acid, was added 0.5 g of 20% palladium on carbon,* and air was expelled from the apparatus by passing nitrogen through for 10-15 minutes. The bath was heated with Wood's alloy to 200°, the flask with the substances then lowered into the alloy and rapidly brought to a temperature of 270°, at which temperature hydrogen began to evolve.

After 35 minutes 300 ml of hydrogen had been collected, liberation of hydrogen then slowing down. Heating was continued for 1 hour and 45 minutes at a bath temperature of 270-320°. The termination of reaction was judged by the volume of collected hydrogen. Upon cooling, the contents of the flask were dissolved in ether, and removed from the catalyst by filtration. The ether solution was washed was 10 % NaOH and then acidified with 10 % hydrochloric acid. A small precipitate, 0.3 g , separated, m.p. 119-120°.

Ether was distilled off from the ether solution and to the butyrated residue were added 12.3 g KOH and 40 ml of alcohol, and the reaction mixture was heated for 6 hours. After termination of the heating, the alcohol was distilled off, and the remainder diluted with water and acidified with 10% hydrochloric acid. The separated precipitate was filtered off and recrystallized from a mixture of benzene and alcohol. 2.7 g of substance, m.p. 119-121°, was obtained.

3.241 mg substance; 8.830 mg CO_2; 1.966 mg H_2O. Found %: C 74.30; H 6.79. $C_{16}H_{18}O_3$.
Calculated %: C 74.42; H 6.97.

b) Dehydration of the ethyl ester of β-(2-ethoxytetrahydronaphthoyl-3)-propionic acid was carried out as in the preceding experiment. 5 g of the ethyl ester of the ketoacid and 0.2 g of 20% palladium on carbon were taken for reaction. Heating was continued for 3.5 hours at 290-310°. After cooling, the contents of the flasks were dissolved in ether, the catalyst filtered off, and the ether solution washed with 10% hydrochloric acid, upon which there separated a resinous precipitate, which was recrystallized from a mixture of benzene and alcohol (more alcohol was taken than benzene). After repeated recrystallizations from benzene, there was obtained 0.2 g of substance, m.p. 119-121°. The earlier-separated ether layer was dried with sodium sulfate. After distillation of the ether, a resinous substance remained, which underwent saponification with alcoholic alkali.

Elementary analysis of the substance with m.p. 119-121° has shown that, by contents, this substance corresponds to 2-ethoxynaphthylbutyric acid.

3.464 mg substance: 9.485 mg CO_2; 2.159 mg H_2O. Found %: C 74.68; H 6.98. $C_{16}H_{18}O_3$.
Calculated %: C 74.42; H 6.97.

2-Hydroxy-3-naphthylbutyric acid. Desalkylation of γ-(2-ethoxy-3-naphthyl)-butyric acid, obtained by dehydration of the ethyl ester of γ-(2-ethoxytetrahydronaphthyl-3)-butyric acid followed by saponification of the ethyl ester, was effected in the following manner. 3.5 g of 2-ethoxynaphthyl-3-butyric acid, 70 ml of glacial acetic acid, and 113 ml of 48% hydrobromic acid were heated for 3 hours at 110-125°. After cessation of heat, the mixture was steam evaporated to dryness in vacuo. The residue was dissolved in 10% NaOH, the solution filtered off from the undissolved portion, and the filtrate acidified with 10% hydrochloric acid, the separated acid being filtered off and washed with water. After recrystallization from a benzene-alcohol mixture, 2.3 g of substance, m.p. 138-140°, was obtained. After repeated recrystallization, its m.p. was 139-141°.

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* Preparation of the catalyst. To 5 g of activated wood charcoal were added 10 ml of nitric acid, 1.33, and 100 ml distilled water, and the mixture was heated on a water bath. The acid was then poured off, and the carbon was washed first with hot and then with cold water, and then dried for 8 hours at 100°, and for a few hours at 175-180°.

To 2 g of the charcoal, purified by the indicated method, were added 35 ml of distilled water and 0.8 g of palladium chloride, dissolved by heating in 6 ml of water and 0.5 ml concentrated hydrochloric acid. After passing hydrogen with shaking, into the suspension to the point of discoloration of the liquid, the palladium was filtered off, washed first with hot distilled water and then with cold until there was no chloride in the wash water, then subsequently with alcohol, ether, and finally dried in a vacuum dessicator over alkali.

4.173 mg substance: 11.159 mg CO_2; 2.200 mg H_2O. 3.995 mg substance: 10.680 mg CO_2; 2.198 mg H_2O. Found %: C 72.93, 72.91; H 6.17, 6.15. $C_{14}H_{18}O_3$. Calculated %: C 73.04. H 6.09.

Upon desalkylation of 2-ethoxy-3-naphthylbutyric acid, which was obtained by dehydration of the ethyl ester of 2-ethoxytetrahydro-3-naphthoylpropionic acid with subsequent saponification of the ester, there was taken 0.2 g of 2-ethoxy-3-naphthylbutyric acid, 4 ml of glacial acetic acid, and 6.5 ml of 48% hydrobromic acid. After the usual treatment and recrystallization of the separated substance, its m.p. was 139-141°. The analytical data corresponded to the composition of hydroxynaphthylbutyric acid.

4.432 mg substance: 11.960 mg CO_2; 2.359 mg H_2O. Found %: C 73.59; H 5.95. $C_{14}H_{14}O_3$. Calculated %: C 73.04; H 6.09.

Ethyl ester of γ-(2-hydroxynaphthyl-3)-butyric acid. To 1.8 g of γ-(2-hydroxynaphthyl-3)-butyric acid were added 20 ml of absolute alcohol, 1 ml of concentrated sulfuric acid, and the mixture was heated for 6 hours. After completion of the reaction, the alcohol was distilled off, the residue diluted with water and extracted with ether, and the ether solution washed with 3% aqueous sodium bicarbonate, then with water, and dried with sodium sulfate. After removal of the ether, 1.5 g of precipitate was obtained from the small volume remaining; after double recrystallization from petroleum ether, the m.p. of the substance was 70-71°.

3.850 mg substance: 10.498 mg CO_2; 2.329 mg H_2O. Found %: C 74.37; H 6.77. $C_{16}H_{18}O_3$. Calculated %: C 74.42; H 6.97.

Oxidation of β-(2-ethoxytetrahydronaphthoyl-3)-propionic acid. ar-2-Ethoxy-3-tetrahydronaphthoic acid. 18 g of sodium hydroxide dissolved in 30 ml of water was placed into an ice-cooled flask; into this alkaline solution was passed chlorine to an excess weight of 12 g. The resultant sodium hypochlorite solution was heated to 50°, with mechanical stirring, and to it was gradually added 2 g of β-(2-ethoxytetrahydronaphthoyl-3)-propionic acid dissolved in 15 ml of 40% sodium hydroxide solution. After addition of the ketoacid, stirring and heating were continued for 3 hours at 70°. The reaction mixture was left overnight and then the precipitated sodium salt of 2-ethoxytetrahydronaphthyl-3-carboxylic acid was filtered off. To the substance obtained was added water, and to the suspension was added, with thorough mixing, 10% hydrochloric acid to the point of acid reaction to Congo. The separated substance was filtered off and recrystallized three times from alchohol. Yield 0.6 g with m.p. 118-120°.

3.875 mg substance: 10.045 mg CO_2; 2.496 mg H_2O. Found %: C 70.56; H 7.20. $C_{13}H_{16}O_3$. Calculated %: C 70.80; H 7.27.

Desalkylation of ar-2-ethoxytetrahydro-3-naphthoic acid. Ar-2-Hydroxy-3-tetrahydronaphthoic acid. To 1.7 g of 2-ethoxytetrahydronaphthoic acid were added 34 ml of glacial acetic acid and 55 ml of 48% hydrobromic acid. The reaction mixture was heated for 3 hours at 110-125° and evaporated to dryness in vacuo. The residue was dissolved in 10% NaOH solution, filtered off from the undissolved portion, and the filtrate acidified with 10% hydrochloric acid. 12 g of substance was obtained, m.p. 176-179°. After double recrystallization from a benzene-alcohol mixture, its m.p. was 181-182°. *

3.671 mg substance: 9.191 mg CO_2; 2.080 mg H_2O. Found %: C 68.28; H 6.33. $C_{11}H_{12}O_3$. Calculated %: C 68.75; H 6.25.

Methyl ester of 2-hydroxy-3-tetrahydronaphthoic acid. To 0.6 g of 2-hydroxytetrahydro-3-naphthoic acid were added 10 ml of absolute methanol, 0.5 ml of concentrated sulfuric acid, and the mixture heated for 6 hours. The alcohol was then distilled off; the remainder was diluted with water and treated with ether; the ether solution was washed with 3% sodium bicarbonate solution, then with water, and dried with sodium sulfate. The ether was distilled off. The residue was recrystallized from alcohol, m.p. 41-42.5°. According to Schroeter, the m.p. of the methyl ester of 2-hydroxytetrahydro-3-naphthoic acid was 42°.

4.245 mg substance: 10.886 mg CO_2; 2.556 mg H_2O. Found %: C 69.93; H 6.73. $C_{12}H_{14}O_3$. Calculated %: C 69.90; H 6.84.

SUMMARY

1. The structure of 2-ethoxy-(5,6,7,8)-tetrahydronaphthoyl-3-propionic acid has been defined more accurately by its oxidation to 2-ethoxy-3-tetrahydronaphthoic acid and by further transformation of the latter into compounds of

* 2-Hydroxy-3-tetrahydronaphthoic acid was obtained by Schroeter using other methods. The indicated m.p. in one instance was 176-177°, in another, 182°.

already established structure.

2. Dehydration of the ethyl ester of 2-ethoxy-(5,6,7,8)-tetrahydronaphthyl-3-butyric acid was carried out in the presence of palladium on carbon.

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MESO-ANTHRANILPROPIONIC ACIDS

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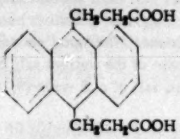
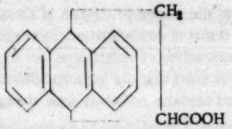
In 1940, A. G. Slobodsky and V. I. Khmelevsky [1] reported that attempts to synthesize β,β'-(anthranil-9,10)-dipropionic acid (I) by heating anthracene with acrolein, with subsequent oxidation, yielded, instead, α,β-endo-(9,10-dihydroanthranil-9,10)-propionic acid (II). The authors indicated that this reaction takes place only in the presence of SO_2, and that all attempts to connect acrolein with anthracene in the absence of sulfurous acid were unsuccessful. (This appeared to be a singular observation, because it is known [2] that the presence of SO_2



(I)

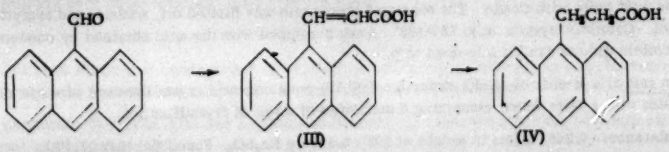


(II)

as a catalyst is indispensable only when acrolein condenses with compounds that possess sufficiently reactive hydrogen atoms, as the result of which condensation are formed β-substituted derivatives of propionic aldehyde.) On the contrary, in diene synthesis in which acrolein participates, as in the example under investigation where acrolein and anthracene interact with the formation, after oxidation, of endodihydroanthranilpropionic acid (II), the presence of a catalyst is usually unnecessary. Indeed, acid (II) is also easily obtained by heating anthracene with acrylic acid or, even more conveniently with β-halogen-propionic acid [3].

The author conducted experiments involving condensation of anthracene with acrolein under the conditions described by Slobodsky and Khmelevsky, both with and without the presence of SO_2 catalyst, demonstrating that the presence of sulfurous acid does not play an essential role in this reaction. In both instances, after oxidation of the reaction product with silver oxide in alkaline medium, there was isolated one and the same α,β-endo-(9,10-dihydroanthranil-9,10)-propionic acid, identical with the acid obtained by heating anthracene with β-bromopropionic acid in cymene.

If anthracene reacted with acrolein in such a way that one atom of hydrogen in the meso position, and the anthracene residue, added to the double bond of acrolein, then oxidation of the reaction product should yield a substance isomeric with acid (II) – β-(anthranil-9)-propionic acid (IV). For confirmation of the structure of the acrolein interaction product, this acid, not described in the literature, was synthesized by the author according to the following scheme:



(III) (IV)

Upon condensation of 9-anthraldehyde with acetic anhydride in the presence of potassium acetate, there was obtained β-(anthranil-9)-acrylic acid (III) in the form of yellow needles, m.p. 246-247°. It is worthy of attention that in the presence of freshly melted sodium acetate there is almost no formation of acid (III).

It is of interest to note that the few literature references to β-(anthranil-9)-acrylic acid are extremely contradictory. Davis and Carmack [4], as a result of condensation of 9-anthraldehyde with malonic acid, obtained 9-anthralmalonic acid, m.p. about 145°, which easily decarboxylated at 180-190° to form β-(anthranil-9)-acrylic acid. The latter, identical with the one synthesized by the author, had an m.p. of 246-247°. Conversely, Fieser

and Hartwell [5], also condensing 9-anthraldehyde with malonic acid, obtained only the acid with m.p. 240-246°, to which they attributed the structure of 9-anthralmalonic acid. The authors were unable to decarboxylate this acid, despite many attempts on their part. Judging from the m.p. of the obtained substance and its unusual resistance to decarboxylation, it can be assumed that, under the conditions of condensation of 9-anthraldehyde with malonic acid, decarboxylation occurred simultaneously, as the result of which Fieser and Hartwell obtained not anthralmalonic acid, but β-(anthranil-9)-acrylic acid. However, this normal assumption is contradicted by the data quoted in the article by the mentioned authors for the analysis of both the acid proper and its "dimethyl" ester, m.p. 134.5-135.5°. It should be noted that the methyl ester of β-(anthranil-9)-acrylic acid obtained by the present author had an m.p. of 110-111°. All of these data permit expression of serious doubt as to the reliability of the result obtained by Fieser and Hartwell.

As a result of reduction of β-(anthranil-9)-acrylic acid with sodium amalgam in aqueous medium, there was obtained β-(anthranil-9)-propionic acid (IV) in the form of thick yellow crystals, m.p. 190-191°.

The presence of color, as a rule, is characteristic for mesoderivatives of anthracene of this type, while the endo compounds of type (II) are usually colorless. In addition to this distinctive characteristic of β-(anthranil-9)-propionic acid, as well as that of β-(anthranil-9)-acrylic acid, is the fact that their sodium salts in aqueous solution are very susceptible to the action of oxygen of the air. Upon standing, these solutions become turbid comparatively quickly as the result of oxidation and formation of anthraquinone. The same phenomenon is observed among other analogous derivatives of anthracene, for example in the case of the sodium salt of anthracene-9-carboxylic acid [6]. On the contrary, the aqueous solution of the sodium salt of α,β-endo-(9,10-dihydroanthranil-9,10)-propionic acid is stable and remains colorless upon storage.

EXPERIMENTAL

α,β-Endo-(9,10-dihydroanthranil-9,10)-propionic acid (II).

a) Condensation of anthracene with acrolein. A mixture of 2 g of pure anthracene and 2 g of acrolein, stabilized by hydroquinone, was heated in a sealed tube for 3 hours at 130°. After completion of the reaction, the yellow-brown liquid was diluted with a small volume of alcohol and poured into five times the volume of water. To the formed emulsion was added a solution of 6 g of silver nitrate in 25 ml of water, followed by 30 ml of 10% sodium hydroxide solution. The mixture was heated and the precipitate filtered off and washed with hot water. The filtrate, together with the wash waters, was shaken with ether for the removal of the neutral admixtures, and after separation of the ether layer was acidified with hydrochloric acid to the point of acidity to Congo. A yellowish precipitate settled out, weight 0.3 g, and was purified by reprecipitation from alkaline solution and animal charcoal. After recrystallization from 50% methanol, colorless crystals were obtained, m.p. 187-188°. The presence of 1 drop of aqueous sulfurous acid, containing 1 mg SO_2, did not affect the result. The yield of crude acid was 0.55 g.

3.317 mg substance: 9.916 mg CO_2; 1.668 mg H_2O. Found %: C 81.53; H 5.63. $C_{17}H_{16}O_2$. Calculated %: C 81.6; H 5.6.

b) Condensation of anthracene with β-bromopropionic acid. A mixture of 0.89 g of anthracene, 1.15 g of β-bromopropionic acid and 3.0 ml of p-cymene was heated at boiling for 7 hours. Upon cooling, the mixture was diluted with ether and extracted with 3% potassium hydroxide solution. The alkaline solution was refiltered and acidified to the acid point with Congo. The separated precipitate was filtered off, washed, and recrystallized from 50% methanol. Colorless crystals, m.p. 187-188°. A sample mixed with the acid obtained by condensing anthracene with acrolein did not exhibit a lowered m.p.

The sodium salt of α,β-endo-(9,10-dihydroanthranil-9,10)-propionic acid crystallizes out of water as long, flat, colorless needles with a satin sheen, containing 6 molecules of water of crystallization.

0.8756 g substance: 0.2467 g loss in weight at 105°; 0.1596 g Na_2SO_4. Found %: H_2O 28.17; Na 5.91. $C_{17}H_{13}O_3Na \cdot 6H_2O$. Calculated %: H_2O 28.4; Na 6.05.

An aqueous solution of the salt remains clear upon standing.

β-(Anthranil-9)-acrylic acid (III)

A mixture of 10 g of 9-anthraldehyde [7], 10 g of acetic anhydride and 5 g of freshly fused potassium acetate was heated with reflux for four hours at 150-160° bath temperature. The reaction mixture was poured into ice water, the precipitate separated, finely pulverized, and washed with water. Upon heating with sodium carbonate, the substance partially dissolved with the formation of a vivid orange solution, which was refiltered and acidified to the

acid point of Congo. A bright yellow precipitate was separated, washed with water and dried. Weight was 6 g. After double recrystallization from propionic acid, yellow needles, m.p. 246-247°, were obtained.

2.712 mg substance: 8.210 mg CO_2; 1.156 mg H_2O. Found %: C 82.46; H 4.77. $C_{17}H_{12}O_2$. Calculated %: C 82.3; H 4.84.

As the result of condensation of anthraldehyde with acetic anhydride, in the presence of freshly fused sodium acetate and a few drops of pyridine, with heating for 9 hours at 160-170°, there separated only about 0.5 g of crude acid.

The sodium salt of β-(anthranil-9)-acrylic acid crystallized from water in the form of orange lamellae. They contained 4 molecules of water of crystallization.

1.1912 g substance: 0.2469 g loss in weight at 105°; 0.2500 g Na_2SO_4. Found %: H_2O 20.73; Na 6.80. $C_{17}H_{11}O_2Na \cdot 4H_2O$. Calculated %: H_2O 21.05; Na 6.73.

Upon recrystallization from alcohol, the sodium salt separated in the form of long yellow needles with 1 molecule of alcohol of crystallization.

1.3488 g substance: 0.1974 g loss in weight at 105°; 0.2964 g Na_2SO_4. Found %: C_2H_5OH 14.64; Na 7.12. $C_{17}H_{11}O_2Na \cdot C_2H_5OH$. Calculated %: C_2H_5OH 14.56; Na 7.28.

An aqueous solution of the salt upon standing rapidly became turbid as the result of oxidation and formation of anthraquinone.

The methyl ester of β-(anthranil-9)-acrylic acid was obtained by the action of dimethylsulfate upon the alkaline solution of the acid. After double recrystallization from acetic acid – bright yellow needles, m.p. 110-111°.

3.246 mg substance: 9.833 mg CO_2; 1.622 mg H_2O. Found %: C 82.62; H 5.59. $C_{18}H_{14}O_2$. Calculated %: C 82.4; H 5.34.

β-(Anthranil-9)-propionic Acid (IV)

To a suspension of 3 g of β-(anthranil-9)-acrylic acid in 500 ml of water, with vigorous stirring was gradually added 50 g of 2.5% sodium amalgam. After completion of the reaction the aqueous solution was filtered and acidified, whereupon there separated a voluminous yellow precipitate. The precipitate was separated, washed with water, dried (weight 2.4 g) and recrystallized several times from acetic acid. Dense, bright yellow crystals, m.p. 190-191°.

4.860 mg substance: 14.510 mg CO_2; 2.464 mg H_2O. 0.2249 g substance: 9.0 ml 0.1 N. NaOH. Found %: C 81.42; H 5.63; M 249.9. $C_{17}H_{14}O_2$. Calculated %: C 81.6; H 5.60; M 250.

From the mother liquor was separated a small amount of anthraquinone, evidently formed by the action of oxygen upon the alkaline solution of the acid.

The sodium salt of β-(anthranil-9)-propionic acid crystallizes from water in the form of pale yellow needles, an aqueous solution of this salt, upon standing, rapidly becomes turbid, but if freshly boiled water is used and the solution kept under nitrogen, it will remain clear.

SUMMARY

1. It has been shown that condensation of anthracene with acrolein, carried out in accordance with the diene- type of synthesis, does not require the presence of sulfurous acid as catalyst.

2. β-(Anthranil-9)-acrylic acid and β-(anthranil-9)-propionic acids and some of their derivatives have been synthesized and characterized.

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SOME SYNTHESES IN THE 4-ACETAMINOBENZALDEHYDE SERIES

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Of numerous synthetic compounds possessing antitubercular activity, which have been studied over the past years, of great interest are the thiosemicarbazones of aromatic aldehydes, and in particular, the thiosemicarbazone of 4-acetaminobenzaldehyde [1,2]. This compound has already been introduced into the medical practice [3,4] of several countries. In this connection it is of great interest to obtain a series of other derivatives of aminobenzaldehyde, among them those with substitutions in the aromatic ring.

To obtain 2- and 3-substituted para-aminobenzaldehydes, it is most convenient to utilize the reaction of oxidation-reduction, which results in 2- and 3- substituted paranitrotoluenes by interaction in an alcoholic solution of alkaline sulfide. By this method, for example, are easily obtained 2- and 3-methoxy-4-aminobenzaldehydes, 2-chlor-4-aminobenzaldehyde and a series of others [5,6], but this reaction does not proceed in the presence of the hydroxyl or the amino group in the 2-position, which is free or easily freed by hydrolysis. In the last case, almost complete reduction of the nitro group to the amino group is observed. In the case of 2-benzyl-hydroxy-nitrotoluene, only a small amount of 2-benzylhydroxy-4-aminobenzaldehyde is obtained by interaction with alkaline sulfide. The main direction of the reaction apparently being that of reduction to substituted paratoluidine. To obtain substituted 4-aminobenzaldehyde, with a second amino group in the ring, nitration of 4-acetamino-3-nitrobenzaldehyde was carried out, according to Cohn and Springer [7], and the 4-acetamino-3-nitrobenzaldehyde obtained was reduced catalytically to 4-acetamino-3-aminobenzaldehyde, from which was obtained 3,4-diacetaminobenzaldehyde.

From 2- and 3-methoxy-4-aminobenzaldehydes were prepared their succinyl- and benzoyl-amino derivatives. From these aldehydes were obtained the thiosemicarbazones.

2-Methoxy-4-acetaminobenzaldehyde served for the authors as the starting material for the synthesis of 2-hydroxy-4-aminohydrocinnamic acid, which is of interest as a homolog of para-aminosalicylic acid – a substance endowed with high antitubercular activity. 2-Methoxy-4-acetaminobenzaldehyde was condensed with malonic acid in the presence of alcoholic ammonia, and after decarboxylation there was obtained 2-methoxy-4-acetaminocinnamic acid, which was hydrogenated in the presence of elementary nickel catalyst, and the resulting 2-methoxy-4-acetaminohydrocinnamic acid, after boiling with 48% hydrobromic acid, in glacial acetic acid, was converted to 2-hydroxy-4-aminohydrocinnamic acid.

EXPERIMENTAL

4-Acetamino-2-methoxybenzaldehyde. To 10 g of the methyl ether of 4-nitro-2-cresol in 40 ml of alcohol, there was added, over a period of three hours of boiling a solution of 6 g of sulfur in 85 ml of 12% aqueous sodium hydroxide. After one hour of heating, the alcohol and water were vaporized off by steam. Upon cooling, the separated 4-amino-2-methoxybenzaldehyde was filtered off and then treated with 5% hydrochloric acid. The hydrochloride of 4-amino-2-methoxybenzaldehyde obtained was acetylated with acetic anhydride in the presence of sodium acetate and glacial acetic acid. The 4-acetamino-2-methoxybenzaldehyde, recrystallized from water, had an m.p. of 143-144° (m.p. is 145° according to the literature).

4-Amino-2-methoxybenzalthiosemicarbazone, m.p. 163-164° (from alcohol).

4.907 mg substance: 5.132 mg $BaSO_4$. Found %: S 14.35. $C_9H_{12}ON_4S$. Calculated %: S 14.27.

4-Acetamino-2-methoxybenzalthiosemicarbazone, after recrystallization from alcohol, had an m.p. of 211-212°.

4.372 mg substance: 3.859 mg $BaSO_4$. Found %: S 12.12. $C_{11}H_{14}O_2N_4S$. Calculated %: S 12.02.

4-Acetamino-2-benzylhydroxybenzaldehyde. To 12 g of the benzylether of 4-nitro-2-cresol in 50 ml of

ethanol, during a period of three hours, while boiling, there was added a solution of 5.14 g of sulfur in 75 ml of 12% sodium hydroxide. The alcohol and water were distilled off with steam. The greenish-brown precipitate of polymeric aldehyde was separated (7 g) and acetylated by acetic anhydride in the presence of sodium acetate and glacial acetic acid. After treatment of the acetylated product with water followed by heating to boiling, from the filtrate, upon cooling, was separated 0.32 g of yellowish crystals, m.p. 95-100°, giving a positive test for the aldehyde group with ammoniacal silver, and forming, with an aqueous solution of thiosemicarbazide, a thiosemicarbazone.

4-Acetamino-2-benzylhydroxybenzalthiosemicarbazone after recrystallization from alcohol had an m.p. of 199-201°.

5.273 mg substance: 3.434 mg $BaSO_4$. Found %: S 8.94. $C_{17}H_{18}O_2N_4S$. Calculated %: S 9.35.

The residue from the acetylation, in the amount of 5 g, was recrystallized from glacial acetic acid, and a substance was obtained, m.p. 74°, which did not give a melting point depression for the mixed sample with the benzyl ether of 4-nitro-2-cresol. From the mother liquor a substance was obtained which, upon double recrystallization from alcohol, gave 1.57 g of 4-acetamino-2-benzylhydroxytoluene with an m.p. of 116-120°.

8.185 mg substance: 0.397 ml N_2 (21°, 738 mm). 7.665 mg substance: 0.380 ml N_2 (23.5°, 738 mm). Found %: N 5.47, 5.49. $C_{16}H_{17}O_2N$. Calculated %: N 5.49.

4-Acetamino-3-aminobenzaldehyde. 2 g of 4-acetamino-3-nitrobenzaldehyde, obtained by nitration of 4-acetaminobenzaldehyde [7], was hydrogenated in 35 ml of alcohol in the presence of 4 g of elementary nickel catalyst. In 1 hour the theoretical volume of hydrogen (600 ml) was consumed. After the removal of the catalyst, the solution was concentrated in vacuo. The residue was treated with a hot solution of 10% hydrochloric acid, and the hydrochloride of 4-acetamino-3-aminobenzaldehyde was obtained.

5.635 mg substance: 0.686 ml N_2 (24.5°, 728 mm). Found %: N 13.38. $C_9H_{11}O_2N_2Cl$. Calculated %: N 13.06.

4-Acetamino-3-aminobenzalthiosemicarbazone was prepared by mixing an aqueous solution of thiosemicarbazide with an alcoholic solution of 4-acetamino-3-aminobenzaldehyde, obtained by catalytic hydrogenation. M.p. 320° (with decomposition).

4.679 mg substance: 4.338 mg $BaSO_4$. Found %: S 12.73. $C_{10}H_{13}ON_5S$. Calculated %: S 12.74.

3,4-Diacetaminobenzalthiosemicarbazone. After hydrogenation of 4 g of 4-acetamino-3-nitrobenzaldehyde, followed by removal of the solvent in vacuo, the crude 4-acetamino-3-aminobenzaldehyde was acetylated with 10 ml of acetic anhydride. The 3,4-diacetaminobenzaldehyde was separated in the form of its thiosemicarbazone. 3,4-Diacetaminobenzalthiosemicarbazone had the form of dark red crystals, m.p. 275-276°.

3.831 mg substance: 3.047 mg $BaSO_4$. Found %: S 10.92. $C_{12}H_{15}O_2N_5S$. Calculated %: S 10.92.

4-Succinylamino-2-methoxybenzaldehyde. 0.5 g of 4-amino-2-methoxybenzaldehyde in 10 ml of chloroform was heated with 0.4 g of succinic anhydride for 1.5 hours with a reflux. The separated solid was reprecipitated from bicarbonate solution with 5% hydrochloric acid solution, and after double recrystallization from water-alcohol (30%) had the appearance of yellow crystals, m.p. 193-194°. 4-Succinylamino-2-methoxybenzaldehyde was difficultly soluble in water, readily soluble in alcohol. Yield 0.2 g.

7.334 mg substance: 0.381 ml N_2 (27.5°, 730 mm). Found %: N 5.67. $C_{12}H_{13}O_5N$. Calculated %: N 5.55

4-Succinylamino-2-methoxybenzalthiosemicarbazone after recrystallization from 60% alcohol had an m.p. of 189-190°.

3.757 mg substance: 2.756 mg $BaSO_4$. Found %: S 10.16. $C_{13}H_{18}O_4N_6S$. Calculated %: S 9.87.

4-Succinylamino-3-methoxybenzaldehyde. 0.45 g of 4-amino-3-methoxybenzaldehyde [6] in 8 ml of chloroform was heated with 0.3 g of succinic anhydride for 2 hours on a water bath with a reflux condenser. The separated precipitate was purified by reprecipitation from bicarbonate solution by 5% hydrochloric acid solution. 4-Succinylamino-3-methoxybenzaldehyde, after recrystallization from water, had an m.p. of 178-179°. Yield 0.5 g.

4.208 mg substance: 0.209 ml N_2 (27.5°, 732.0 mm). Found %: N 5.43. $C_{12}H_{13}O_5N$. Calculated %: N 5.55.

4-Succinylamino-3-methoxybenzalthiosemicarbazone, after recrystallization from 60% alcohol, had an m.p. of 200-201°.

3.790 mg substance: 2.814 mg $BaSO_4$. Found %: S 10.19. $C_{14}H_{16}O_4N_4S$. Calculated %: S 9.87.

4-Amino-3-methoxybenzalthiosemicarbazone was obtained by mixing a hot alcoholic solution of 4-amino-3-methoxybenzaldehyde with a hot aqueous solution of thiosemicarbazide, and after recrystallization from alcohol had an m.p. of 160-161°.

4.026 mg substance: 4.254 mg $BaSO_4$. Found %: S 14.50. $C_9H_{11}ON_4S$. Calculated %: S 14.27.

4-Acetamino-3-methoxybenzalthiosemicarbazone was obtained upon mixing an alcoholic solution of 4-acetamino-3-methoxybenzaldehyde with a hot aqueous solution of thiosemicarbazide, which, after recrystallization from alcohol, had an m.p. of 232-233°.

4.588 mg substance: 4.053 mg $BaSO_4$. Found %: S 12.13. $C_{11}H_{14}O_2N_4S$. Calculated %: S 12.02.

4-Benzoylamino-3-methoxybenzalthiosemicarbazone. 0.5 g of 4-amino-3-methoxybenzaldehyde in 4 ml of 10% potassium hydroxide solution was shaken for three hours with 0.45 g of benzoyl chloride. The precipitate which separated after the heated-up reaction mass had cooled was isolated and washed with alcohol and ether. Upon mixing an alcoholic solution of 4-benzoylamino-3-methoxybenzaldehyde with a hot aqueous solution of thiosemicarbazide, there separated 4-benzoylamino-3-methoxybenzalthiosemicarbazone, which, after crystallization from alcohol, melted at 250° (with decomposition).

4.509 mg substance: 3.226 mg $BaSO_4$. Found %: S 9.82. $C_{16}H_{18}O_2N_4S$. Calculated %: S 9.75.

4-Acetamino-2-methoxycinnamic acid. A mixture of 2 g of 4-acetylamino-2-methoxybenzaldehyde and 1.08 g of malonic acid was heated on a water bath with 4.5 ml of 8% alcoholic ammonia to the formation of a clear, colorless solution. The alcohol from the reaction mixture was distilled off, and heating was continued until the evolution of CO_2 ceased. The residue was treated with 15-20 ml of hot water. Upon acidification of the alkaline solution with 5% hydrochloric acid solution the substance precipitated in the form of a yellow solid. After crystallization from 60% alcohol, the 4-acetamino-2-methoxycinnamic acid had an m.p. of 229-230°. Yield 0.75 g. Readily soluble in organic solvents, poorly in water.

7.200 mg substance: 0.394 ml N_2 (27.5°, 729.5 mm). Found %: N 5.96. $C_{12}H_{13}O_4N$. Calculated %: N 5.95.

4-Acetamino-2-methoxyhydrocinnamic acid. 1.55 g of 4-acetamino-2-methoxycinnamic acid in 75 ml of 5% sodium carbonate solution was hydrogenated in the presence of elementary nickel catalyst. The theoretical volume of hydrogen (150 ml) was absorbed over a period of 1 hour. Upon acidification with 5% hydrochloric acid solution, 4-acetamino-2-methoxycinnamic acid separated, which, after crystallization from 50% alcohol, had an m.p. of 168-169°. Soluble in alcohol and acetone, partially in ether, insoluble in water.

6.270 mg substance: 0.341 ml N_2 (20.5°, 726 mm). Found %: N 5.96. $C_{12}H_{15}O_4N$. Calculated %: N 5.90.

4-Amino-2-hydroxyhydrocinnamic acid. 3.5 g of 4-acetamino-4-methoxyhydrocinnamic acid in 75 ml of glacial acetic acid was heated with 75 ml of hydrobromic acid, for 3 hours at 135-140°. Volatile acids were removed in vacuo. The dry residue of 4-amino-2-hydroxyhydrocinnamic acid hydrobromide was treated with ethyl acetate, and purified by reprecipitation with absolute ether from a concentrated solution in absolute ethanol. Yield 2 g; m.p. 189-190°. The hydrobromide of 4-amino-2-hydroxyhydrocinnamic acid had the appearance of small, colorless crystals, soluble in water, alcohol and acetone, partially so in ethyl acetate, insoluble in ether.

0.1312 g substance: 4.93 ml 0.1 N $AgNO_3$. Found %: Br 30.03. $C_9H_{12}O_3NBr$. Calculated %: Br 30.50.

SUMMARY

1. A series of aromatic aldehydes was obtained, containing the acetamino group in position 4, together with substitution in position 2 or 3; the thiosemicarbazones of these aldehydes were obtained.

2. Upon interaction of 4-amino-2- and 3-methoxybenzaldehydes with succinic anhydride or benzoyl chloride, the corresponding acylated compounds were obtained.

3. Syntheses of 4-acetamino-2-methoxycinnamic acid, 4-acetamino-2-methoxyhydrocinnamic acid and 4-amino-2-hydroxyhydrocinnamic acid were described.

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THE SYNTHESIS OF CERTAIN p-ALKYLSULFONYLBENZALDEHYDES

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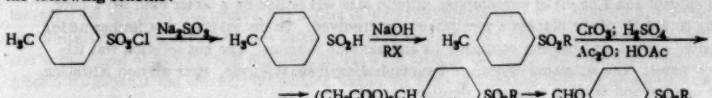
As is known, the oxidation of p-nitrotoluene with chromic anhydride, in the presence of glacial acetic acid, acetic anhydride and concentrated sulfuric acid, yields p-nitrobenzaldehyde [1]. Lately it has been determined that in a similar manner the oxidation of certain aryl-p-tolylsulfones yields p-arylsulfonylbenzaldehydes [2]. The outstanding advantage of this reaction appears to be the fact that the reaction stops at the aldehyde stage, because, at the rate of formation of the latter, there occurs transformation into the diacetate, which is resistant to further oxidation. Up to the present, however, it has remained unclarified whether if this method is applied to the oxidation of alkyl-p-tolylsulfones, the action of the oxidizer in this case will be mainly directed upon the methyl group of the tolyl radical, or whether the aliphatic sulfone radical will be seriously affected.

A series of experiments conducted by the authors has indicated that this method is fully applicable for the preparation of p-alkylsulfonylbenzaldehydes [3]. Of this series of compounds, up to now there has been described only p-methylsulfonylbenzaldehyde, obtained in 1945 [4] from acetanilide in 7 steps, the last of which consisted of transforming p-methylsulfonylbenzonitrile into the aldehyde by the action of anhydrous lead chloride in ether solution.

The course worked out by the authors for synthesis of the alkylsulfonylbenzaldehyde series is expressed by the following scheme:



where R = CH_3; C_2H_5; C_4H_9; C_8H_{13}; CH_2COOH.

p-Toluene sulfochloride, by sodium sulfite reduction at 60-80°, was transformed into p-toluenesulfinic acid [5] with a yield of 98% of theoretical. By condensing the sodium salt of this acid with alkyl halides in water-alcohol medium, with 16-22 hours heating, the corresponding alkyl-p-tolylsulfones were obtained, which underwent oxidation with excess chromic anhydride in a mixture of glacial acetic acid, acetic anhydride and concentrated sulfuric acid. The reaction was carried out with cooling and with vigorous stirring so that the temperature would not exceed +5° to +9°, for otherwise the yield of aldehyde was reduced. Treatment with aqueous acetic acid frequently led to the formation of resinous chromic complexes, which also resulted in considerable reduction of yield.

The great advantage of the method given for obtaining alkylsulfonylbenzaldehydes is the fact that alkyl-p-tolylsulfones can undergo oxidation without prior purification, since the major part of the admixture separates easily during the course of the reaction.

Upon pouring the reaction mass into ice water, the diacetates of the aldehydes separate out in the form of colorless crystalline compounds, with the exception of the p-hexylsulfonylbenzaldehyde diacetate which comes out as an oily liquid. After saponification of the aldehyde diacetates with sulfuric acid in water-alcohol medium, the free aldehydes obtained were: p-methyl-, p-ethyl-, p-butyl- and p-hexyl-sulfonylbenzaldehydes. For their characterization, the corresponding thiosemicarbazones were prepared.

Upon oxidation, under analogous conditions, of p-tolylsulfonylacetic acid, there was obtained benzaldehyde-p-sulfonylacetic acid – p-carboxymethylsulfonylbenzaldehyde. It is of interest to note that upon carrying out the condensation of the sulfinic acid sodium salt with chloracetic acid, there separated out of the mother liquor from p-tolylsulfonylacetic acid a crystalline substance which was found to be p,p'-ditolyldisulfoxide [7]. Both the diacetate of p-carboxymethylsulfonylbenzaldehyde and the aldehyde itself represent non-crystallizing substances. It was impossible to obtain the aldehyde in completely pure form since it easily decomposes upon heating. For characterization of this aldehyde, the thiosemicarbazone was made.

EXPERIMENTAL

Hexyl-p-tolylsulfone. A mixture of 16 g p-toluenesulfinic acid with 40 ml of water was neutralized with 10% NaOH solution to a weak alkaline reaction to methyl red indicator, and to the solution were added 90 ml of alcohol and 17 ml of hexyl bromide. The mixture was boiled on a water bath for 23 hours, and the solvent then removed by distillation; water was added to the remainder, and the separated light yellow oil was extracted with ether. The ether solution was washed with water and dried with potash. There remained, after distillation of the ether, a yellowish mobile liquid, hexyl-p-tolylsulfone, which was redistilled in vacuo; b.p. 158-159° at 0.8 mm. Yield 16 g.

0.1955 g substance: 0.1897 g $BaSO_4$. Found %: S 13.32. $C_{13}H_{20}O_2S$. Calculated %: S 13.33.

Oxidation of methyl-p-tolylsulfone. To the solution of 11.48 g methyl-p-tolylsulfone (obtained by the condensation of the sodium salt of p-toluenesulfinic acid with methyl iodide [8]) in 106 ml glacial acetic acid and 105 ml acetic anhydride, with ice cooling and rapid stirring, 15.8 ml of concentrated sulfuric acid was added dropwise at such a rate that the temperature did not exceed +10°. To the reaction mixture was further added slowly, with cooling and stirring, 19 g of dry powdered chromic anhydride at a temperature from +7° to +9°, after which the mixing was continued for 10-15 minutes. The reaction mixture was poured onto 600 g of ice, and to the mixture was added 400 ml of water. The separated precipitate was filtered off, washed with ice water, and with vigorous stirring was treated with 50 ml of 2% sodium bicarbonate; the precipitate was further washed with water and dried in a vacuum dessicator.

Yield of the p-methylsulfonylbenzaldehyde diacetate was 9.44 g. After recrystallization from 96% alcohol, its m.p. was 135-137°.

4.100 mg substance: 7.557 mg CO_2; 1.882 mg H_2O. Found %: C 50.27; H 5.13. $C_{12}H_{14}O_6S$. Calculated %: C 50.33; H 4.93.

p-Methylsulfonylbenzaldehyde. A mixture of 8 g of the diacetate of p-methylsulfonylbenzaldehyde, 15.5 ml of water, 15.5 ml of alcohol and 1.55 ml of concentrated sulfuric acid was boiled on a water bath for 1 hour. At the end of the heating period all of the diacetate precipitate was dissolved. To the solution was further added a small amount of activated carbon, and heating continued for another 5-10 minutes. The hot solution was filtered and cooled with ice water. The separated crystals of p-methylsulfonylbenzaldehyde, after suction filtration, were washed with dilute alcohol and dried in a vacuum dessicator.

Yield 3.25 g. After recrystallization from aqueous alcohol, the substance had an m.p. of 156-158° (according to the literature, 157° [4]).

Thiosemicarbazone of p-methylsulfonylbenzaldehyde — almost colorless crystals; m.p. 232° (with decomposition).

0.2117 g substance: 0.3672 g $BaSO_4$. Found %: S 25.00. $C_9H_{11}O_2N_3S_2$. Calculated %: S 24.90.

Oxidation of ethyl-p-tolylsulfone. To a solution of 5.5 g of ethyl-p-tolylsulfone (obtained by condensation of the sodium salt of p-toluenesulfinic acid with ethyl bromide [9]) in a mixture of 47.5 ml of glacial acetic acid and 47 ml of acetic anhydride there was gradually added 7.1 ml of concentrated H_2SO_4 at a temperature not exceeding +10°. Then 8.5 g of chromic anhydride was gradually added. The experiment was carried out under the same conditions as was shown above for the oxidation of methyl-p-tolylsulfone. After treatment of the reaction mixture there was separated 5 g of p-ethylsulfonylbenzaldehyde diacetate (yield 56% of theoretical). Recrystallized from alcohol, the substance had an m.p. of 107-108°.

2.876 mg substance: 5.499 mg CO_2; 1.378 mg H_2O. Found %: C 52.15; H 5.36. $C_{13}H_{16}O_6S$. Calculated %: C 52.00; H 5.33.

p-Ethylsulfonylbenzaldehyde. A mixture of 5 g of the diacetate of p-ethylsulfonylbenzaldehyde, 10.4 ml of alcohol, 10.4 ml of water and 1.04 ml of concentrated sulfuric acid was boiled on a water bath for 0.5 hours. After treatment with carbon, followed by filtration and cooling, there separated 2.66 g of p-ethylsulfonylbenzaldehyde with an m.p. of 105-106.5°. Yield 82% of theoretical.

For the purpose of analysis the substance was recrystallized from 30% alcohol.

3.404 mg substance: 6.840 mg CO_2; 1.471 mg H_2O. Found %: C 54.80; H 4.83. $C_9H_{10}O_3S$. Calculated %: C 54.54; H 5.05.

Thiosemicarbazone of p-ethylsulfonylbenzaldehyde – light yellow crystals; m.p. 223-224°.

4.175 mg substance: 7.150 mg $BaSO_4$. 6.175 mg substance; 0.825 ml N_2 (17°, 733 mm). Found %: S 23.51; N 15.16. $C_{10}H_{13}O_2N_3S_2$. Calculated %: S 23.34; N 15.50.

Oxidation of butyl-p-tolylsulfone. To a solution of 8 g of butyl-p-tolylsulfone (obtained by condensation of the p-toluenesulfinic acid sodium salt with butyl bromide [10]) in a mixture of 57 ml of glacial acetic acid and 58 ml of acetic anhydride there was gradually added 8.5 ml of concentrated sulfuric acid and then 11 g of chromic anhydride. The experiment was carried out under the above-described conditions. After the usual treatment there was isolated 6.57 g of p-butylsulfonylbenzaldehydediacetate; recrystallized from alcohol, the substance had an m.p. of 106-108°.

3.951 mg substance: 7.933 mg CO_2; 2.229 mg H_2O. Found %: C 54.76; H 6.31. $C_{15}H_{24}O_6S$. Calculated %: C 54.87; H 6.09.

p-Butylsulfonylbenzaldehyde. A mixture of 6 g of p-butylsulfonylbenzaldehydediacetate, 10 ml of alcohol, 10 ml of water and 1 ml of concentrated sulfuric acid was boiled on a water bath for 1 hour. Upon cooling there separated from the solution an oil. The mixture was poured into water, extracted with ether, the ether solution washed with water and dried with sodium sulfate. The residue, after removal of the solvent was found to be a difficultly-crystallizable oily liquid, giving a characteristic aldehyde reaction with ammoniacal silver solution.

Upon mixing an alcoholic solution of this aldehyde with a hot aqueous solution of thiosemicarbazide, there was obtained the semicarbazone, m.p. 184-185°.

0.0744 g substance: 0.1148 g $BaSO_4$. Found %: S 21.19. $C_{12}H_{17}O_2N_3S_2$. Calculated %: S 21.39.

Oxidation of hexyl-p-tolylsulfone. To a solution of 13 g of hexyl-p-tolylsulfone in a mixture of 85 ml acetic anhydride and 85.5 ml of glacial acetic acid, there was added 13 ml of concentrated sulfuric acid, and later, 15 g of chromic anhydride. The reaction was carried out under the above-shown conditions. After completion of the chromic anhydride addition, the reaction mixture was stirred for another 10-15 minutes at room temperature and then was poured into 1 liter of water containing ice. Immediately an oil separated which did not crystallize. The substance was extracted with ether, the ether solution then washed several times with water, and with excess of bicarbonate dissolved in water, to remove the acetic acid and then dried with calcined potash. After distillation of the solvent, the residue was in the form of a yellow, oily liquid with a sharp odor. Weight 11 g. Even after considerable cooling, the substance did not crystallize.

p-Hexylsulfonylbenzaldehyde. A mixture of 11 g of p-hexylsulfonylbenzaldehyde diacetate obtained from an earlier experiment, 40 ml of alcohol, 15 ml of water and 1.8 ml of concentrated sulfuric acid was boiled on a water bath for 1 hour; the alcohol was then distilled off in vacuo, and water was added to the residue. The separated oil was extracted with ether, the ether solution washed with water and dried with anhydrous sodium sulfate. After distilling off the solvent, the residue (9.7 g) was redistilled in vacuo.

p-Hexylsulfonylbenzaldehyde appears in the form of a viscous, colorless liquid, m.p. 151-152° at 0.3 mm.

0.1667 g substance: 0.1529 g $BaSO_4$. Found %: S 12.59. $C_{13}H_{18}O_3S$. Calculated %: S 12.54.

Thiosemicarbazone – slightly yellowish crystals, m.p. 182-184°.

0.1266 g substance: 0.1781 g $BaSO_4$. Found %: S 19.34. $C_{14}H_{21}O_2N_3S_2$. Calculated %: S 19.45.

Oxidation of p-tolylsulfonylacetic acid. To a solution of 7.7 g of p-tolylsulfonylacetic acid (obtained by condensation of monochloracetic acid with p-toluenesulfinic acid [6]) in a mixture of 57 ml glacial acetic acid and 56.5 ml of acetic anhydride was added dropwise, with cooling and stirring, 8.5 ml of concentrated sulfuric acid, followed by 11 g of chromic anhydride at a temperature from +6 to +8°. Upon completion of the chromic anhydride addition, the mixture was poured into 600 g of water with ice. The aqueous solution was extracted several times with ether, the ether extracts dried with anhydrous sodium sulfate; the ether and acetic acid were removed in vacuo. The remaining non-crystallizable oily liquid (6.82 g) was dissolved in 11 ml of alcohol, and to the solution was added 11 ml of water and 1.1 ml of concentrated sulfuric acid. After heating the mixture on a water bath for 1 hour, the alcohol and the ethyl acetate formed were removed by distillation; to the remainder was added water, and the separated oil extracted with ether. The ether solutions were twice washed with water, dried with anhydrous sodium sulfate and the solvent removed in vacuo. The residue – benzaldehyde-p-sulfonylacetic acid – appeared as a yellow oily-like liquid, giving a characteristic aldehyde reaction with ammoniacal silver solution, and was dissolved in bicarbonate. When an attempt was made to distill it in vacuo, the substance decomposed.

Thiosemicarbazone of benzaldehyde-p-sulfonylacetic acid – yellowish crystals, soluble in bicarbonate; m.p. 228-229°.

0.1107 g substance: 0.1709 g $BaSO_4$. Found %: S 21.19. $C_{10}H_{11}O_4N_3S_2$. Calculated %: S 21.40.

SUMMARY

A method for the preparation of p-alkylsulfonylbenzaldehydes has been worked out, consisting of the oxidation of alkyl-p-tolylsulfones by chromic anhydride in the presence of glacial acetic acid, acetic anhydride and concentrated sulfuric acid.

A series of p-alkylsulfonylbenzaldehydes and their derivatives was obtained.

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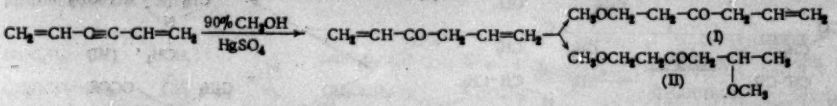
DERIVATIVES OF ACETYLENE. 146. HETEROCYCLIC COMPOUNDS

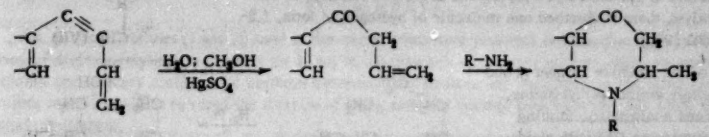
XXII. REACTION OF PRIMARY AMINES WITH 1,5-DIMETHOXYHEXANE-3-ONE AND WITH 7-METHOXY-5-ISOBUTYL-1,5-HEPTADIENE-4-ONE

I. N. Nazarov and S. A. Vartanyan

It has been shown in the preceding reports [1,2] that divinylacetylene, when heated with aqueous methanol in the presence of mercury sulfate, hydrates smoothly with the formation of vinylallyl ketone which, under the conditions of the experiment, will add one or two molecules of methanol, giving a mixture of methoxy ketones (I and II), with a predominance of 1,5-dimethoxyhexan-3-one (II):



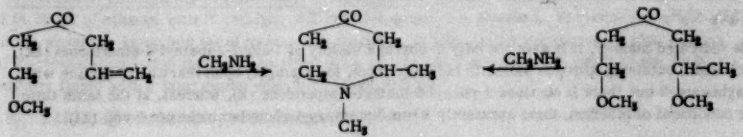
Recently there was worked out, in the authors' laboratory, a new simple method for the synthesis of γ-piperidones [3], by way of interaction of ammonia and primary amines with vinylallyl ketones which are easily obtained by the hydration of divinylacetylenic hydrocarbons in aqueous methanol:



These simple reactions connect acetylene with the diverse compounds of the piperidinic series, to which belong many important, naturally-occurring alkaloids, giving a wide range of possibilities for the syntheses of new physiologically-active substances, in particular, those of analgesic and anesthetic actions.

For the purpose of further working out these important reactions, the authors investigated the reaction of primary amines with vinylallyl ketone and its corresponding methoxy ketones (I and II), obtained by hydration of divinylacetylene.

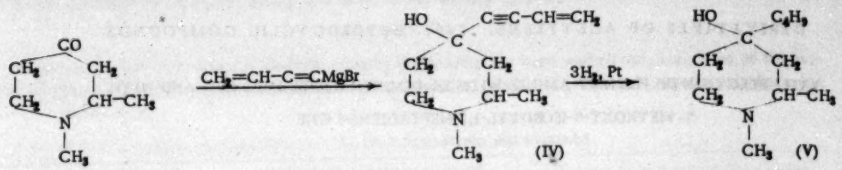
Upon reaction of an aqueous solution of methylamine acetate with methoxyketones (I and II), there was obtained, in 60% yield, the above-described [3] 1,2-dimethyl-4-piperidone (III):



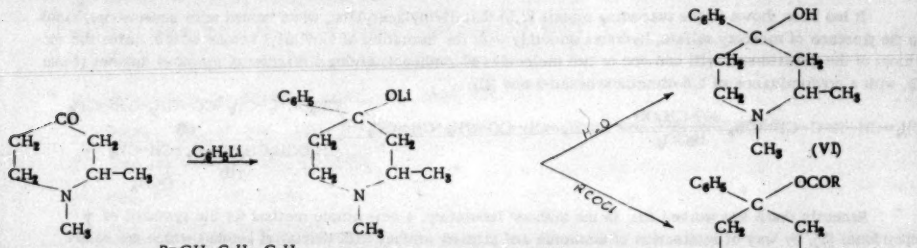
(I) (III) (II)

Unlike other γ-piperidones, 1,2-dimethyl-4-piperidone is completely unable to enter into condensation with acetylene and vinylacetylene in the presence of pulverized potassium hydroxide, because it so quickly solidifies into a hard insoluble product [4]. However, the reaction of magnesiumbromovinylacetylene [5] with 1,2-dimethyl-4-piperidone proceeds normally and leads to the formation of 1,2-dimethyl-4-vinylethenyl-4-

piperidol (IV) which, upon hydrogenation with Pt catalyst, absorbs 3 molecules of hydrogen and converts into 1,2-dimethyl-4-butyl-4-piperidol (V):

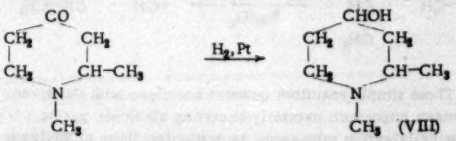


Upon reaction of lithiumphenyl [6] with 1,2-dimethyl-4-piperidone, there is obtained the lithium alcoholate of the tertiary alcohol, which, upon decomposition with water, yields 1,2-dimethyl-4-phenyl-4-piperidol (VI), and by reaction with acid anhydrides, forms the corresponding esters (VII):

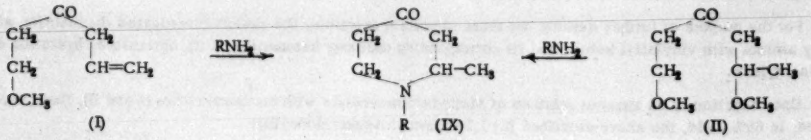


R= CH_3, C_2H_5, C_6H_5.

Upon reduction of 1,2-dimethyl-4-piperidone in alcohol solution, in the presence of Pt catalyst, there is absorbed one molecule of hydrogen to form, 1,2-dimethyl-4-piperidol (VIII):

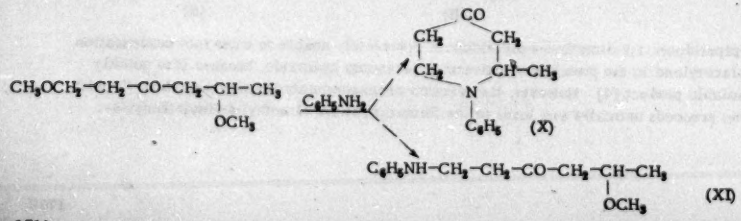


Reactions of the methoxy ketones (I and II) with higher primary amines (ethyl-amine, propylamine) proceed analogously, forming corresponding γ-piperidones (IX) with yields up to 30%.



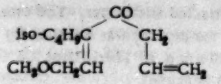
R = C_2H_5, C_3H_7

In the indicated manner, it is easy not only to obtain a variety of 1-alkyl-2-methyl-4-piperidones (IX), but also compounds containing nitrogen aromatic radicals. Thus, for example, upon reaction of aniline with 1,5-dimethoxyhexane-3-one there is obtained 1-phenyl-2-methyl-4-piperidone (X), whereas, at the same time, under milder conditions of reaction, there apparently forms 5-methoxy-1-phenylaminohexan-3-one (XI):

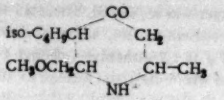


In one of the preceding articles [7] the authors described the obtaining of dienone (XII), which, upon reaction with ammonia, easily formed piperidone (XIII), containing a methoxyl group in the side chain.

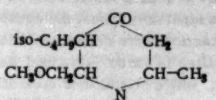
Upon reaction of methylamine with 7-methoxy-5-isobutyl-1,5-heptadiene-4-one (XII) there is obtained in good yield 1,2-dimethyl-5-isobutyl-6-methoxymethyl-4-piperidone (XIV):



(XII)



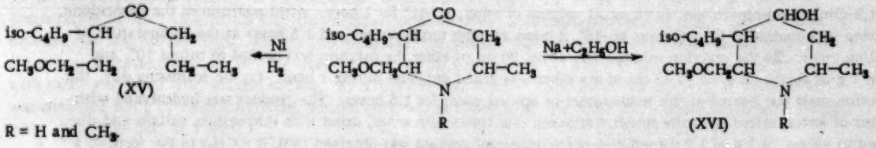
(XIII)



(XIV)

Piperidones (XIII) and (XIV), in contrast to γ-piperidones (not containing the methoxyl group) are completely incapable of condensing with acetylene in the presence of powdered potassium hydroxide [8], and also in liquid ammonia. Condensation does not take place between piperidone (XIV) and lithium phenyl when the reaction mass is heated for three hours at the boiling temperature of ether.

Upon catalytic hydrogenation in an autoclave at 120 atm. and 150° in the presence of Ni catalyst, piperidones (XIII and XIV) split, with the formation of a saturated ketone and ammonia or methylamine. However, upon reduction of piperidone (XII) with sodium in alcohol, there was obtained in high yield the corresponding secondary piperidol (XVI, R = H):



(XV)

(XVI)

R = H and CH_3.

EXPERIMENTAL

The methoxy ketones (I and II) used in the experiments were prepared as described previously [1,2] by hydration of divinylacetylene in aqueous methanol in the presence of mercury sulfate. Because, upon reaction of ammonia and primary amines with methoxy ketones (I and II) there are obtained one and same products, it is therefore more expedient to react the mixture of these methoxy ketones without subjecting them to previous fractional distillation.

1,2-Dimethyl-4-piperidone (III). A 30 g mixture of methoxyketones (I and II) (b.p. 83-87° at 9 mm; n_D^{20} 1.4300), 30 ml of glacial acetic acid, 30 g of 30% aqueous solution of methylamine and 10 ml of dioxane was vigorously mixed by an automatic stirrer at 60° for 5.5 hours. The solution was neutralized with 20% hydrochloric acid to a weak acid reaction, and the neutral products extracted with ether. The organic bases were salted out with potash, extracted with ether, dried with sodium sulfate and distilled in vacuo. 13 g of the earlier described [3] 1,2-dimethyl-4-piperidone (III) was obtained in the form of a mobile liquid, turning yellow on standing, with a characteristic amine odor, b.p. 80-83° at 10 mm; n_D^{20} 1.4583. From the neutral products there was obtained 3.1 g of the original ketones (b.p. 76-79° at 6 mm; n_D^{20} 1.4291).

Reduction of 1,2-dimethyl-4-piperidone. 4.7 g of freshly distilled 1,2-dimethyl-4-piperidone was hydrogenated in 15 ml of ethanol with Pt catalyst. 800 ml of hydrogen was absorbed. For reduction of the carbonyl group to the alcoholic group 800 ml of hydrogen is required. Hydrogenation was complete after 6 hours. As the result of fractional distillation there was obtained 3.9 g of 1,2-dimethyl-4-piperidol (VIII) in the form of a transparent mobile liquid with a faint amine odor; b.p. 78-80° at 3 mm.

n_D^{20} 1.4750; d_4^{20} 0.9554; MR_D 38.10; calculated 37.91.

The hydrochloride of this alcohol is represented as a white powder, m.p. 185-187°.

1.970 mg substance: 0.592 ml 0.02 N $AgNO_3$. 3.438 mg substance: 1.045 ml 0.02 N $AgNO_3$.
Found %: Cl 21.30; 21.55. $C_7H_{15}N \cdot HCl$. Calculated %: Cl 21.45.

1,2-Dimethyl-4-phenyl-4-piperidol (VI). In a round-bottomed flas, equipped with mechanical stirrer, dropping funnel and reflux condenser, was prepared a solution of phenyllithium in a nitrogen atmosphere from

1 g of small fragments of lithium and 13 g of bromobenzene in 50 ml of absolute ether. To the phenyllithium obtained in this manner was added dropwise, during 1.5 hours at 0° temperature, 7.3 g of 1,2-dimethyl-4-piperidone, dissolved in an equal volume of ether. Stirring was continued for two more hours at room temperature and 1.5 hours at boiling temperature of ether. The product was hydrolyzed with 10 ml of water, and after careful shaking in a separatory funnel the aqueous layer was separated, saturated with potash and extracted with ether. The ether extractions were combined, dried by sodium sulfate, and after driving off the ether, the product was fractionally distilled in vacuo. Obtained was 4.3 g of 1,2-dimethyl-4-phenyl-4-piperidol (IV) with a b.p. of 129-131° at 2.5 mm, which crystallized upon dilution with ether, and melted at 123-124° (from light benzene).

12.25 mg substance: 34.31 mg CO_2; 10.47 mg H_2O. 9.13 mg substance: 25.59 mg CO_2; 7.86 mg H_2O. Found %: C 76.45, 76.50; H 9.54, 9.64. $C_{13}H_{19}ON$. Calculated %: C 76.09; H 9.21.

1,2-Dimethyl-4-phenyl-4-piperidol is readily soluble in acetone, alcohol and benzene, poorly so in water; its hydrochloride upon standing in air liquifies.

The acetate of 1,2-dimethyl-4-phenyl-4-piperidol (VII, R = CH_3). In a three-necked round-bottomed flask, equipped with mecanical stirrer and mercury seal, a dropping funnel, a tube for introducing nitrogen (the whole reaction being conducted in nitrogen atmosphere), and a thermometer, there were placed 50 ml of absolute ether and 1.1 g of small lithium fragments. To this mixture was added 2 g of bromobenzene and, reaction started, 10 more g of bromobenzene was gradually added, dissolved in 10 ml of ether. The reaction mixture was then heated for 1.5 hours at the temperature of boiling ether. To the phenyllithium prepared in this manner, was added 9 g of 1,2-dimethyl-4-piperidone, in an equal volume of ether, at -15° for 1 hour. After addition of the piperidone, mixing was continued for 1.5 hours at -15°, 2 hours at room temperature, and 1.5 hours at the temperature of boiling ether. To the reaction mixture was added 30 ml of ether, the mixture was cooled to minus 10°, and then 7 g of acetyl chloride in 15 ml of dry ether was added dropwise during 1 hour. On the following day, the reaction mass was heated at the temperature of boiling ether for 1.5 hours. The product was hydrolyzed with 10 ml of water, salted out with potash, extracted four times with ether, dried with magnesium sulfate and distilled in vacuo. 2.1 g of 1,2-dimethyl-4-phenylpiperidol acetate was obtained (VII, R = CH_3) in the form of a yellowish liquid with ammoniacal odor; b.p. 123-125° at 2 mm; n_D^{20} 1.5171; d_4^{20} 1.0510; MR_D 70.93; calculated 71.13).

Upon mixing this acetate with a saturated alcoholic solution of picric acid, the picrate was obtained in the form of a brown powder, m.p. 157-158° from alcohol.

3.298 mg substance: 0.363 ml N_2 (26°, 738 mm). 3.048 mg substance: 0.335 ml N_2 (26°, 737 mm). Found %: N 12.20, 12.17. $C_{21}H_{24}O_9N_4$. Calculated %: N 11.76.

Upon recovery the hydrochloride of the acetate liquefies in absolute ether and precipitates out in the form of a non-crystallizable oil.

Propionate of 1,2-dimethyl-4-phenyl-4-piperidol. (VII, R = C_2H_5). To the phenyllithium, prepared, as described above, from 2.2 g of metallic lithium and 25 g of brombenzene in a solution of 50 ml of absolute ether, was added dropwise at a temperature of -10° over a period of 1 hour, 15 g of 1,2-dimethyl-4-piperidone in an equal volume of absolute ether. On the following day the reaction mixture was again stirred for 3 hours at the temperature of boiling ether, and to the mixture was added dropwise 30 g of propionic acid anhydride, Stirring was then continued for 1 hour at room temperature and 3 hours at the temperature of boiling ether. The product was treated with water (30 ml), salted out with potash, extracted with ether, dried with sodium sulfate and fractionally distilled in vacuo. 5.5 g of the propionate of 1,2-dimethyl-4-phenyl-4-piperidol was obtained (VII, R = C_2H_5) in the form of a yellow liquid, darkening upon standing; b.p. 128-130° at 2 mm.

n_D^{20} 1.5165; d_4^{20} 1.0400; MR_D 75.90; calculated 75.74.

13.02 mg substance: 35.14 mg CO_2; 10.45 mg H_2O. 13.35 mg substance: 35.88 mg CO_2; 10.60 mg H_2O. Found %: C 73.66, 73.35; H 8.91, 8.85. $C_{16}H_{23}O_2N$. Calculated %: C 73.56; H 8.81.

Picrate – Light yellow, fine crystals, with an m.p. of 150-151° from alcohol.

Tartrate. 0.3 g of the propionate was dissolved in 5 ml of dry acetone and a solution of 0.2 g of tartaric acid in 3 ml of acetone was added. After removal of the acetone, there remained a thick mass, which, upon washing with ether, became hard and brittle; softening point 100-108°. Upon attempting to recrystallize from other solvents, the product separated in the form of an oil.

Benzoate of 1,2-dimethyl-4-phenyl-4-piperidol (VII, R = C_6H_5). To the phenyllithium, prepared, as described above, from 1.2 g of small lithium fragments and 15.4 g of bromobenzene in 50 ml of absolute ether, 10 g of 1,2-dimethyl-4-piperidone in an equal volume of ether was added dropwise at a temperature of -10°. After the addition of piperidol, mixing was continued for 2 hours at a temperature of -10°, 4 hours at room temperature and 2 hours at the temperature of boiling ether. After dilution of the reaction mixture with 50 ml of ether, the mixture was cooled to -12°, and to it added, dropwise, with stirring, 20 ml of benzoyl chloride in a solution of 30 ml of ether. Stirring was continued an additional 2 hours at room temperature and the reaction mixture left for the night. On the following day, the mixture was stirred for 2 hours at the temperature of boiling ether. The product was hydrolyzed with water (20 ml), salted out with potash, extracted three times with ether, dried with sodium sulfate and fractionally distilled in vacuo. 3.2 g of the benzoate of 1,2-dimethyl-4-phenyl-4-piperidol (VII, R = C_6H_5) was obtained in the form of a very viscous oil, b.p. 144-148° at 2 mm. Upon standing, there precipitated from this oil crystals, m.p. 155-156° (from carbon tetrachloride).

6.452 mg substance: 0.284 ml N_2 (26°, 738 mm). 5.308 mg substance: 0.225 ml N_2 (24°, 739 mm). Found %: N 4.72, 4.88. $C_{20}H_{23}O_2N$. Calculated %: N 4.53.

1,2-Dimethyl-4-vinylethyl-4-piperidol (IV). In a round-bottomed flask, equipped with mechanical stirrer, dropping funnel and reflux condenser, ethylmagnesium bromide was prepared from 10 g of magnesium and 50 g of ethyl bromide in a solution of 70 ml absolute ether. Into the ether solution of ethylmagnesium bromide, with cooling by cold water, there was passed, for 1 hour, 30 g of vinylacetylene. The reaction mass was stirred for 2 hours at room temperature, and 1 hour at the boiling temperature of ether, to complete the evolution of ethane. To the magnesiumbromovinyl acetylene obtained in this manner, there was added over a period of 3 hours at a temperature of -10°, 15 g of 1,2-dimethyl-4-piperidone, dissolved in an equal volume of ether, and the reaction mixture was left for the night. On the following day, the product was hydrolyzed with 18% hydrochloric acid (15 ml) at a temperature of -10°, the aqueous layer of the base was salted out with potash, extracted five times with ether and dried with sodium sulfate. As a result of fractional distillation of the product in vacuo, there was obtained 5.3 g of vinylacetylenepiperidol (IV), which appeared in the form of a viscous liquid with a base odor, b.p. 100-102° at 3 mm.

6.962 mg substance: 0.461 ml N_2 (23°, 743 mm). 6.669 mg substance: 0.432 ml N_2 (23°, 743 mm). Found %: N 7.47, 7.31. $C_{11}H_{17}ON$. Calculated %: N 7.82.

The hydrochloride of this alcohol precipitated in the form of a viscous, non-crystallizable mass.

Hydrogenation of 1,2-dimethyl-4-vinylethyl-4-piperidol. 2.7 g of freshly distilled vinylacetylenepiperidol (IV) in a solution of 18 ml of ethanol was hydrogenated in the presence of Pd catalyst. In 1 hour, 1 liter of hydrogen was absorbed, and 72 ml more was absorbed slowly. For the full hydrogenation of one triple, or of two double, bond(s) is required 1.08 liters of hydrogen. As a result of fractional distillation of the hydrogenated product, there was obtained 2.17 g of butylpiperidol (V), in the form of a clear, viscous liquid, with a characteristic base smell; b.p. 96-97° at 3 mm.

11.30 mg substance: 29.30 mg CO_2; 12.54 mg H_2O. 9.27 mg substance: 23.94 mg CO_2; 10.47 mg H_2O. Found %: C 70.76, 70.48; H 12.42, 12.64. $C_{11}H_{23}ON$. Calculated %: C 71.35; H 12.40.

1-Phenylamino-5-methoxyhexan-3-one (XI). A mixture of 10 g of 1,5-dimethoxyhexan-3-one (II), 10 g of freshly distilled aniline, 5 ml of water and 15 ml of dioxane was heated in a flas at 100° for 10 hours. The solution was neutralized with dilute hydrochloric acid to a weak acid reaction, and, after extraction of the neutral products, the organic bases were salted out with potash, extracted with ether, dried with sodium sulfate and fractionally distilled in vacuo. Obtained was 6.1 g of methoxyketamine (XI), b.p. 138-140° at 2.5 mm.

n_D^{20} 1.5315; d_4^{20} 1.0820; MR_D 63.41; calculated 63.86.

7.770 mg substance: 0.456 ml N_2 (23°, 746 mm). 7.780 mg substance: 0.437 ml N_2 (23°, 746 mm). Found %: N 6.36, 6.64. $C_{13}H_{19}O_2N$. Calculated %: N 6.33.

From the ether extraction of neutral products was recovered 2.3 g of 1,5-dimethoxyhexan-3-one.

1-Phenyl-2-methyl-4-piperidone (X). A mixture of 10 g of methoxyketones (I and II) (b.p. 83-87° at 9 mm; n_D^{20} 1.4300), 10 g of freshly-distilled aniline, 5 ml of water and 18 ml of dioxane was heated in a flask at 123-130° for 8 hours. The solution was neutralized with dilute hydrochloric acid to a weak acid reaction, and the neutral products were extracted with ether. The organic bases were salted out with potash, extracted with ether,

dried with sodium sulfate and fractionally distilled in vacuo. Obtained was 4.3 g of 1-phenyl-2-methyl-4-piperidone (X) in the form of a viscous liquid, turning yellow on standing, with an amine odor; b.p. 118-120° at 3 mm.

n_D^{20} 1.5500; d_4^{20} 1.0704; MR_D 56.30; calculated 55.78.

7.710 mg substance: 0.529 ml N_2 (23°, 740 mm). 6.679 mg substance: 0.445 ml N_2 (23°, 740 mm) Found %: N 7.49, 7.70. $C_{12}H_{15}ON$. Calculated %: N 7.41.

From the ether solution of neutral products was recovered 1.2 g of 1,5-dimethoxyhexan-3-one.

1-Propyl-2-methyl-4-piperidone (IX, R = C_3H_7). A mixture of 10 g of methoxyketones (I and II) (b.p. 83-87° at 9 mm n_D^{20} 1.4300), and 10 g of 40% aqueous solution of propylamine was mixed with water cooling (heating up was noticed), and heated on a water bath further at 60° for 1.5 hours, and then treated as in the preceeding experiment. Obtained was 2.3 g of 1-propyl-2-methyl-4-piperidone (IX, R = C_3H_7), in the form of a mobile liquid with an amine odor; b.p. 72-74° at 3 mm.

n_D^{20} 1.4615; d_4^{20} 0.9521; MR_D 44.78; calculated 45.51.

1.569 mg substance: 0.130 ml N_2 (22°, 740 mm). Found %: N 9.30. $C_9H_{17}ON$. Calculated %: N 9.03.

1-Ethyl-2-methyl-4-piperidone (IX, R = C_2H_5). A mixture of 12 g of methoxyketones (I and II) (b.p. 83-87° at 9 mm; n_D^{20} 1.4300), 12 ml of water, 4.5 g of ethylamine and 10 ml of glacial acetic acid was stirred with a mechanical stirrer at a temperature of 60° for 3 hours. The solution was neutralized with 20% hydrochloric acid to a weak acid solution and the neutral products extracted with ether. The organic bases were salted out with potash, extracted with ether, dried with sodium sulfate and fractionally distilled in vacuo. Obtained was 3.4 g of 1-ethyl-2-methyl-4-piperidone (IX, R = C_2H_5), in the form of a mobile liquid, turning yellow upon standing, with a characteristic amine odor; b.p. 67-68° at 3 mm.

n_D^{20} 1.4590; d_4^{20} 0.9420; MR_D 40.9; calculated 40.89.

7.25 mg substance: 1.03 ml 0.05 N $KH(IO_3)_2$. 9.45 mg substance: 1.33 ml 0.05 N $KH(IO_3)_2$. Found %: N 9.92, 9.83. $C_8H_{15}ON$. Calculated %: N 9.93.

The picrate of 1-ethyl-2-methyl-4-piperidone melted at 149-150°.

1,2-Dimethyl-5-isobutyl-6-methoxymethyl-4-piperidone (XIV). A mixture of 28 g of 5-isobutyl-7-methoxy-1,5-heptadiene-4-one (XII) (b.p. 95-97° at 5 mm; n_D^{18} 1.4700) [7] and 35 g of 35% methylamine was heated in a metal flask at 60° for 2 hours. The excess methylamine was driven off on a water bath at 45° in vacuo 70 mm. The solution was neutralized with hydrochloric acid to a weak acid reaction, and the neutral products extracted with ether. The organic bases were salted out by potash, extracted with ether and dried with sodium sulfate, followed by fractional distillation in vacuo. Obtained was 25 g of the piperidone (XIV) in the form of a viscous liquid, turning yellow on standing, with a characteristic amine odor; b.p. 117-119° at 2 mm.

n_D^{20} 1.4750; d_4^{20} 0.9702; MR_D 65.85; calculated 65.62.

10.36 mg substance: 25.96 mg CO_2; 10.04 mg H_2O. 10.28 mg substance: 25.82 mg CO_2; 9.83 mg H_2O. Found %: C 68.38, 68.55; H 10.84, 10.70. $C_{13}H_{25}O_2N$. Calculated %: C 68.72. H 11.01.

The picrate precipitated in the form of a dark, non-crystallizable mass. The hydrochloride was completely unstable, and immediately liquified. From the neutral products of the ether solution was recovered 3.7 g of original ketone (XII) (b.p. 94-98° at 6 mm; n_D^{20} 1.4700).

Hydrogenation of 1,2-dimethyl-5-isobutyl-6-methoxymethyl-4-piperidone. 10 g of freshly distilled piperidone (XIV), b.p. 117-119° at 2 mm; n_D^{20} 1.4750 in 25 ml of ethanol was hydrogenated in the presence of Raney nickel catalyst in an autoclave at a hydrogen pressure of 120 atmospheres and a temperture of 150°. During 4 hours the pressure fell to 8.5 at 150°, in the autoclave. The reduction product, with a strong odor of methylamine, was filtered off from the catalyst and fractionally distilled in vacuo. Upon distillation the following fractions were obtained (at 5 mm): first fraction, b.p. 93-100°; n_D^{20} 1.4373 - 2.7 g; 2 fraction, b.p. 100-127°; n_D^{20} 1.4640 - 0.9 g; 3rd fraction, b.p. 127-132°; n_D^{20} 1.4720 - 5.2 g; resinous sediment 0.8 g.

Upon repeated fractional distillation of the first fraction there was separated the earlier-described 7-methoxy-5-isobutylheptan-4-one (XV) with a b.p. of 118-120° at 18 mm; n_D^{20} 1.4345 [7].

In a similar manner goes the hydrogenation of 2-methyl-5-isobutyl-6-methoxymethyl-4-piperidone (XIII). At a pressure of 85 atmospheres and a temperature of 100°, the piperidone ring is split, and under milder conditions the product does not hydrogenate.

2-Methyl-5-isobutyl-6-methoxymethyl-4-piperidol (XVI, R=H). 16 g of piperidone (XIII) (b.p. 110-112° at 6 mm; n_D^{20} 1.4700) was dissolved in 350 ml of alcohol and 35 g of metallic sodium in small pieces was added slowly. When the sodium was completely dissolved, to the mixture was then added, dropwise, while cooling with ice water, 160 ml of concentrated hydrochloric acid to an acid reaction. The product was filtered off from the sodium chloride, the precipitate washed three times with alcohol, and water, and the water-alcohol solution of the hydrochloride was evaporated off in vacuo to a volume of 40 ml. The remaining viscous oil was neutralized with soda, salted out with potash, extracted with ether, dried with sodium sulfate and fractionally distilled in vacuo. Obtained was 13.6 g of 2-methyl-5-isobutyl-6-methoxymethyl-4-piperidol (XVI, R=H) in the form of a viscous liquid with amine-like odor: b.p. 118-119.5° at 4 mm.

11.66 mg substance: 28.39 mg CO_2; 12.33 mg H_2O. 12.66 mg substance: 30.74 mg CO_2; 13.17 mg H_2O. Found %: C 66.45, 66.32; H 11.84, 11.65. $C_{12}H_{25}O_2N$. Calculated %: C 66.96; H 11.62.

SUMMARY

During the interaction of primary amines with vinylallylketone, or with its corresponding methoxyketones (I and II), obtained by hydration of divinylacetylene in aqueous methanol, there are formed N-substituted 2-methyl-4-piperidones (IX, R= CH_3, C_2H_5, C_3H_7, C_6H_5). Obtained also are 1,2-dimethyl-4-piperidol (VIII), 1,2-dimethyl-4-vinylethenyl-4-piperidol (IV), 1,2-dimethyl-4-butyl-4-piperidol (V), 1,2-dimethyl-4-phenyl-4-piperidol (VI), its esters (VII: R= CH_3, C_2H_5, C_6H_5), 1,2-dimethyl-5-isobutyl-6-methoxymethyl-4-piperidone (XIV) and 2-methyl-5-isobutyl-6-methoxymethyl-4-piperidol (XVI).

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* See Consultants Bureau translation, p. 1895.
** " " " " p. 2267.
*** " " " " p. 1643.

N-ARYLAMIDES OF HYDROXYCARBOXYLIC ACIDS AND THEIR CONVERSION INTO HETEROCYCLIC COMPOUNDS

XVIII. RELATION BETWEEN SAPONIFICATION OF ARYLAMIDES OF α-, β-, AND γ-HYDROXYCARBOXYLIC ACIDS AND THE EASE OF HETEROCYLIC RING CLOSURE

P. A. Petyunin, N. G. Panferova and I. S. Berdinsky

The saponification of arylamides of α-, β-, and γ-hydroxycarboxylic acids was conducted in both acid and in alkaline medium. The percentage of arylamide saponified was determined by the amount of aromatic amine obtained as a result of the reaction. The latter was determined by the sodium nitrite titration method utilized by B. A. Porai-Koshits and coworkers [1], in the study of azomethine hydrolysis reactions. Saponification in alkaline medium was carried out in the following manner. In a flask equipped with a reflux condenser there was placed an accurately-weighed portion of arylamide, 45-60 moles of 10% KOH solution was poured in, and the mixture boiled for one hour. The aromatic amine was quantitatively determined as indicated above. The data obtained are shown in Table 1.

TABLE 1

No.	Formula of anilide	Weight of substance (in g)	0.05 N $NaNO_2$ (in ml)	Saponified arylamide (in %)
1	$C_6H_5NHCOC(OH)(CH_3)_2$	0.0928	5.24	50.54
2	$C_6H_5NHCOC(OH)(C_2H_5)_2$	0.0827	0.35	4.38
3	$C_6H_5NHCOC(OH)(C_5H_{11}\text{-iso})_2$	0.1009	0.4	5.77
4	$p\text{-}CH_3C_6H_4NHCOC(OH)(C_6H_4CH_3\text{-}o)_2$	0.1485	Does not saponify	
5	$C_6H_5NHCOCH_2C(OH)(C_6H_5)_2$	0.1268	0.91	11.33
6	$C_6H_5NHCO(CH_2)_2C(OH)(CH_3)_2$	0.1230	8.6	72.3
7	$C_6H_5NHCO(CH_2)_2C(OH)(CH_2CH=CH_2)_2$	0.1339	7.56	73.1
8	$C_6H_5NHCO(CH_2)_2C(OH)(C_6H_4OCH_3\text{-}o)_2$	0.1950	7.8	78.2

The p-toluidide of o-tolyl acid upon boiling for one hour with 50% KOH solution was only 7.23% saponified, and with 0.5 N alcoholic KOH solution for 1 hr., only 10.3%. The exceptional resistance to hydrolysis of benzylanilide was observed by McKenzu and Duff [2]. Upon boiling with concentrated alkali solution, and even upon melting with solid alkali, the authors [2] did not obtain satisfactory results.

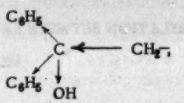
Saponification in acid medium was carried out with the aid of 10% HCl solution. Boiling lasted 1 hour. 50 to 70 moles of acid was taken, depending upon the weight of arylamide taken. The saponification data are given in Table 2.

Upon boiling the p-toluidide of o-tolyl acid with 25% HCl solution, it was only saponified to the extent of 4.83%. Upon lengthy boiling of the p-bromanilide of benzilic acid with 50% H_2SO_4 solution, there was separated a very small amount of 4-bromaniline. It is possible to assume that the reaction goes in the direction of intramolecular condensation with the formation of oxindole derivatives. An experiment performed with the p-phenetidine of benzilic acid and 50% H_2SO_4 solution did not confirm this assumption. Thus the data cited in literature reference [3], referring to the intramolecular condensation of N-ethylbenzilanilide with the aid of 50% H_2SO_4 solution, become doubtful. More concentrated solutions of the acid are not recommended for saponification, in order to avoid possible intramolecular condensation. The mechanics of saponification of esters, and of carboxylic acid amides, are sufficiently explained [4] and the authors do not consider it worth while to dwell upon this question. The difficulty in saponifying the arylamides of benzilic, o-tolyl and diisoamylglycol acids, both in acid and in alkaline medium, should be explained by manifestation of a steric effect, conditioned by the presence at the α-carbon atom of an aromatic and a branched aliphatic radical. The anilide of β,β-diphenyl-β-hydroxypropionic acid (Experiment 5, Tables 1 and 2) saponifies better, because, with the removal of the tertiary alcohol group from the chain, the steric effect is diminished, and the electrochemical effect of the radical begins to appear.

TABLE 2

No.	Formula of anilide	Weight of substance (in g)	0.05 N $NaNO_2$ solution (in ml)	Saponified arylamide (in %)
1	$C_6H_5NHCOC(OH)(CH_3)_2$	0.1000	5.44	48.69
2	$C_6H_5NHCOC(OH)(C_2H_5)_2$	0.1024	3.1	31.33
3	$C_6H_5NHCOC(OH)(C_6H_{11}\text{-iso})_2$	0.1113	0.5	6.54
4	$p\text{-}CH_3C_6H_4NHCOC(OH)(C_6H_4CH_3\text{-}o)_2$	0.1293	Does not saponify	
5	$C_6H_5NHCOCH_2C(OH)(C_6H_5)_2$	0.1389	0.3	3.42
6	$C_6H_5NHCO(CH_2)_2C(OH)(CH_3)_2$	0.1426	12.29	89.26
7	$C_6H_5NHCO(CH_2)_2C(OH)(CH_2CH{=}CH_2)_2$	0.1109	8.56	99.99
8	$C_6H_5NHCO(CH_2)_2C(OH)(C_6H_4OCH_3\text{-}o)_2$	0.2315	8.6	72.6

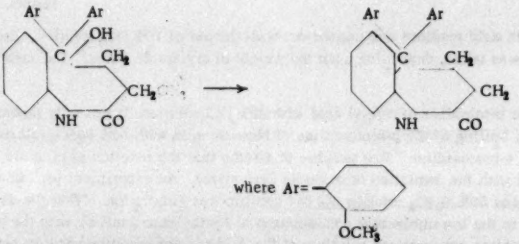
Adjacent to the carbonyl carbon atom of the anilide of β,β-diphenyl-β-hydroxypropionic acid are three groups ($2C_6H_5$– and OH),



possessing –I-effects, and only one group (CH_2) a +I-effect. On the whole, the indicated grouping will attract electrons, according to the mechanism of inductive replacement. This anilide saponifies more readily in alkaline medium because, in accordance with the mechanism of the reaction, the saponification in alkaline medium is speeded up by the presence of the group possessing a minus I-effect.

Arylamides of γ-hydroxycarboxylic acids saponify easily both in acid and in alkaline medium. In the case of radicals with a tertiary alcoholic group, in aryl amides of γ-hydroxycarboxylic acid, an impediment is no longer formed, and the nature of the radicals is of little effect because, with recession over the chain, the force of the inductive effect diminishes to a considerable degree [4]. It was of interest to clarify the relation between ease of saponification of arylamides of hydroxycarboxylic acids and their ability to close the ring. The authors determined [5] that those arylamides condense, which with concentrated sulfuric acid, give a carbonium ion with an electron deficiency on the central carbon atom. From this point of view the authors were interested in those arylamides which have two aromatic radicals at the carbinol carbon atom.

Comparing data obtained by the authors on the saponification of the arylamides of α-, β-, and γ-hydroxycarboxylic acids with their tendency for intramolecular condensation, the following can be noted. Arylamides of α-hydroxycarboxylic acids exhibit selective resistance to saponification both in acid and in alkaline medium; at the same time the heterocylic ring is completed with exceptional ease [6]. Arylamides of β-hydroxycarboxylic acids saponify significantly in alkaline medium and somewhat worse in acid medium. They condense less smoothly [7]. Arylamides of γ-hydroxycarboxylic acids saponify very easily and do not condense. Utilizing the methods worked out by the authors, an attempt was made to close the seven-membered heterocyclic ring in the anilide of γ, γ-bis-2-methoxyphenyl-γ-hydroxybutyric acid according to the following scheme:



To the anilide of γ, γ-bis-2-methoxyphenyl-γ-hydroxybutyric acid was added concentrated sulfuric acid, and the reaction mixture heated on a water bath (80-90°) to full dissolution of the anilide and disappearance of the reddish-violet coloring. Simultaneously the anilide of γ, γ-di-o-methoxydiphenylglycolic acid was completely saponified. Aniline was identified in the form of tribromaniline, m.p. 118° [8], and γ,γ-di-o-methoxydiphenylglycolic acid, after precipitation of sulfuric acid with the aid of $Ba(OH)_2$, and treatment with soda solution, with subsequent evaporation, and crystallization in the form of the sodium salt. The sodium salt dissolved readily in water and with concentrated sulfuric acid gave a red-violet coloration (grouping $Ar_2C(OH)$—).

According to their ease of saponification, arylamides of hydroxycarboxylic acids could be arranged in the

order: $\gamma > \beta > \alpha$. According to their ease of heterocyclic formation, they give the reverse order: $\alpha > \beta > \gamma$ (in the latter the heterocyclic ring does not close). Thus, on the basis of saponification can be foreseen condensation.

SUMMARY

1. The saponification reaction of arylamides of α-, β-, and γ-hydroxycarboxylic acids, both in acid and in alkaline medium, was studied.

2. It was determined that, according to the ease of saponification, the arylamides of the hydroxycarboxylic acids have the order $\gamma > \beta > \alpha$, and according to the ease of heterocyclic ring closure, the reverse order $\alpha > \beta > \gamma$ (the latter not condensing).

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*See Consultants Bureau translation, p. 1029.
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*** " " " p. 1033.

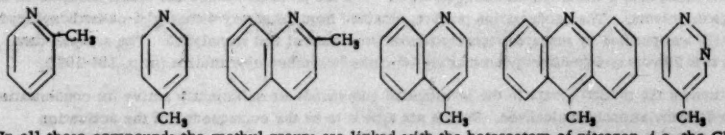
SYNTHESES AND TRANSFORMATIONS OF PYRIMIDINE DERIVATIVES

III. A STUDY OF THE MOBILITY OF HYDROGEN ATOMS OF THE METHYL GROUP IN DERIVATIVES OF MONOHYDROXYDIHYDROPYRIMIDINE

N. V. Khromov-Borisov and A. M. Savchenko

Copious written material pertaining to the study of chemical transformations of pyrimidine compounds, and likewise the results of investigation of derivatives of 4-methyluracil, published by one of the authors with R.S. Karlinskaya [1] demonstrate that the methyl groups arranged on the even positions of the pyrimidine ring possess increased activity. In some cases this activity is so great that the substance appears capable of azo combination reaction at the expense of the hydrogens of the methyl group.

Among the six-membered heterocylic compounds capable of such azo combination are: alkyl halide derivatives of α- and γ-picolines, quinaldine, lepidine and also mesomethylacridine, 5-nitro-4-methyluracil and 5-diazo-4-methyl uracil. It is readily noted that in all these compounds there is a similar arrangement of the methyl group relative to the heteroatoms of nitrogen:



In all these compounds the methyl groups are linked with the heteroatom of nitrogen, i.e. the CH_3 groups are connected to the C=N groups either directly or by the conjugated linkage. This regularity is in complete conformity with electronic concepts concerning the activation mechanism of the CH_3 and CH_2 groups, giving a consistent explanation of the origin of the greater activity of these groups entering into different combinations [2].

A great number of works from the school of academician A. E. Porai-Koshits has been devoted to the study of the reaction ability of the methyl and methylene groups. These works considerably widened the circle of reactions with active methyl and methylene groups and led to the possibility of a theoretical generalization of accumulated regularities. At the present time the authors are correct in expressing the following rule: if the methyl or methylene group is in conjugation with the heteroatom, [illegible] increased activity acquires to its hydrogen atoms. This rule should be called "The A. E. Porai-Koshits Rule", under which name it has been quoted in the works of his students.*

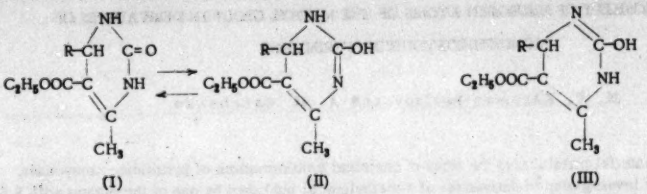
The above-enumerated six-membered heterocyclic compounds possess aromatic character; they contain three double bonds in the ring, upon which the placement of these bonds in the ring is not fixed. If, on the other hand, there could be shown fixation of the double bonds in the molecule of quinaldine or lepidine (after the analogy of naphthalene) then in symmetrical molecules, such as γ-picoline and mesomethylacridine, there would be no substantiation for this hypothesis.

For activation of the methyl group, the presence of three double bonds in the ring is not compulsory from the point of view of the above mechanism. It could even be admitted that in the absence of fixed double bonds in the ring, the binding of a methyl group to the heteroatom to some degree diminishes activation of the methyl group. Up to now, no six-membered heterocyclic compound with two double bonds in the ring and containing an active methyl group has been described. Along this line, we decided to study derivatives of dihydropyrimidine containing the methyl group in position 4.

Fairly easily accessible appear to be the 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidines, containing

* This principle was expressed by N. V. Khromov-Borisov at the meeting of the D. I. Mendeleev All Union Chemical Society on December 6, 1951.

various substitutions in the 6-position. These compounds were obtained for the first time in 1893 by Biginelli [3] by interaction of urea, an aldehyde and acetoacetic ester in absolute alcohol medium and in the presence of concentrated hydrochloric acid. By introducing into the reaction various aldehydes, it was later possible to obtain a whole range of related compounds [4-10]. To them was attributed the following structure (Formula I and II):

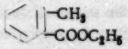


(I) (II) (III)

With such structure the nitrogen heteroatoms cannot activate the methyl group, because the latter is not found in conjugation with them. In addition, the matter is not changed if there is allowed tautomeric displacement of the hydrogen in position 1 (Formula III).

In order to determine whether the above-expressed assumptions are applicable in these cases, the authors decided to study the activity of the methyl groups in two similar compounds (R= H and R= C_6H_5). First of all the authors have established that the compounds studied under sufficiently rigid conditions (melted at 205-210°) are capable of condensing with p-dimethylaminobenzaldehyde. The red products formed are readily soluble in the majority of organic solvents. The condensation product, obtained from 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine (R= H), was purified by repeated reprecipitations from alcohol and reanalyzed. The analysis data confirmed that it is 2-hydroxy-4-(p-dimethylaminostyryl)-5-carbethoxydihydropyrimidine (m.p. 194-198°).

In this manner the methyl groups in the investigated compounds are sufficiently active for condensation reaction with p-dimethylaminobenzaldehyde. Does it not appear to be the consequence of the activation influence of the $COOC_2H_5$ group, being placed in the o-position to the methyl group? But a similar influence is displayed in the known reactions of Claisen and Perkin. To answer this question, the authors proceeded to study the interaction of dihydropyrimidines with diazo compounds. As it is known,

neither $CH_3COOC_2H_5$, nor $CH_3CH{=}CHCOOC_2H_5$, nor 

are capable of entering into azo combination reaction. The methyl groups in these compounds are under the activating influence of the carbethoxyl group; nevertheless, they do not appear sufficiently active (in the relationship) as regards diazo compounds. Thus it could be anticipated that our dihydropyrimidines will also be incapable of azo combination. Otherwise it would have to be considered that upon the methyl group is somehow transmitted the activating influence of the heteroatoms of the dihydropyrimidine ring.

Substituent in position 6	Diazo compound	M.p. of dye	Color of dye	Color in alkaline medium	Color in acid medium
H	$NO_2{-}C_6H_4{-}N{=}N{-}OH$	174-176°	Maroon	Blue	Yellow
C_6H_5	Ditto	155-157	Dark-red	Bright-violet	Yellow
H	$NH_2SO_2{-}C_6H_4{-}N{=}N{-}OH$	Indefinite (above 260°)	Brick-red	Red	Yellow
C_6H_5	Ditto	Indefinite (above 240°)	Brick-red	Raspberry-red	Yellow

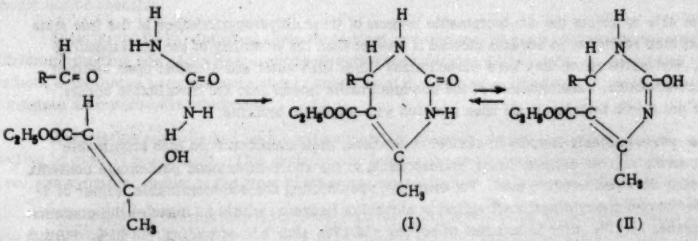
As diazo compounds, the authors took p-nitrodiazobenzene and p-sulfamidodiazobenzene. The reaction was conducted in glacial acetic acid medium, in the presence of anhydrous sodium acetate. It appeared that under these conditions azo combination took place: upon interaction with one mole of the diazo compound,

dyes were obtained, identified as monoazo dyes. The properties of the synthesized azo dyes are cited in the preceding table.

Upon union of the investigated dihydropyrimidines with 2 moles of p-nitrodiazobenzene, there are obtained azo dyes differing in their properties from those quoted in the table. However, they also appear to be monoazo dyes in composition: within the limits of accuracy of the elementary analyses, they do not differ from those quoted in the table. On this basis, it could be assumed that upon reaction of the second molecule of diazo compound there occurs transformation of the dihydropyrimidine nucleus into pyrimidine.

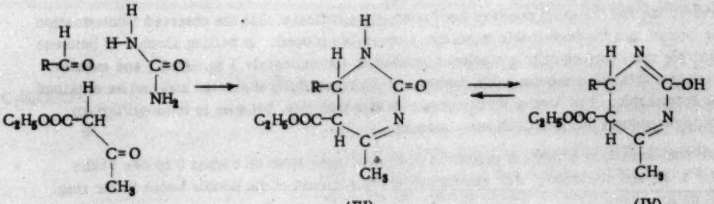
The experimental facts obtained indicate that the methyl group located in the 4-position of the dihydropyrimidines studied possesses great activity, sufficient for interaction with diazo compounds. Further, it will be shown below that this interaction proceeds at the expense of the methyl group. Thus, it should be assumed that the methyl group in these substances is under the activating influence of the dihydropyrimidine ring. However, as we have already seen, the structural formula, suggested by Biginelli for the monohydroxydihydropyrimidines, cannot explain this activating action, inasmuch as the methyl group is not in conjugation with the heteroatoms of the ring.

All these facts and considerations forced the authors to review the question of structure of the investigated dihydropyrimidines. At the time of the structural formula development, Biginelli proceeded from the enol form of acetoacetic ester:



(I) (II)

If it is assumed that acetoacetic ester enters into reaction as the keto form, then the structure of the condensation product will be different:



(III) (IV)

In the compound of such a structure the increased activity of the methyl group becomes understandable, because in it the methyl group is under the activating influence of two groups $>C=N-$. However, it is known that these dihydropyrimidines are capable of combining with two atoms of bromine [11] and this is the argument in favor of Biginelli's structural formula (II). Thus, on the one hand the capability of azo conjugation at the expense of the methyl group necessitates ascribing to these compounds Structure (IV), while on the other hand the capability for bromination necessitates ascribing to them the Structure (II). These facts forced us to assume that the dihydropyrimidines studied represent a mixture of two isomers (II) and (IV).

In addition, the authors were occupied with the experimental verification of their assumption. First of all, it was necessary to determine whether the dibromide has the structure which is ascribed to it. Inasmuch as the investigated compounds contain an active CH_3 group, it was necessary to show that, upon reaction of bromine, there is not substitution of two atoms of hydrogen in the methyl group, but rather linkage of two bromine atoms to the two adjacent carbon atoms. The authors carried out bromination of the investigated dihydropyrimidines (R=H and R=C_6H_5).

Experiment has shown that the obtained dibromides, upon debromination with the aid of zinc dust, transformed into primary dihydropyrimidines. This indicates the presence of two bromine atoms on adjacent carbon atoms. Thus the structure of the dibromides corresponds to the structural Formula (II).

During execution of these experiments it was noticed that the bromination required severe conditions (boiling in chloroform with large excess of bromine) and did not give quantitative yields. This unusual difficulty in bromination cannot be satisfactorily explained by the formula of Biginelli (II), which contains the double bond in position 4-5. Compound (II) should very easily, in the cold, add two atoms of bromine to the double bond C=C, while the compound with structure (IV) should not possess this characteristic. Upon this assumption the authors decided to determine the content percentage of isomer (II) in the dihydropyrimidines studied, by the application of bromometric titration. The determination was conducted in the following manner: to an alcoholic solution of the substance was added in the cold an excess of freshly prepared and titrated alcoholic bromine. The remaining bromine, after addition of potassium iodide, was titrated with hyposulfite, and thus was determined the percentage content of brominated isomer (II).

It was found that at both 0° and 17°, notwithstanding a large excess of bromine (3 moles for 1 mole of substance), bromination proceeds only to a defined limit. This limit is practically obtained within 5 minutes and does not change upon prolonged bromination. Thus the authors determined that 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine contains 6-7% of the brominated isomer, and 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine — 19-21%.

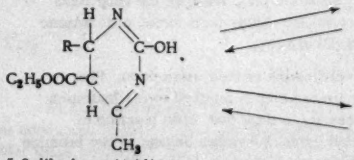
The authors were able to isolate the non-brominable isomers of these dihydropyrimidines in the free state by utilizing the fact that their solubility in aqueous alcohol is smaller than the solubility of the corresponding 4,5-dibromoderivatives. For purification, they were washed many times with water and alcohol; upon attempt to recrystallize from alcohol partial transformation of the non-brominable isomer into the brominable occurs. The isolated isomers do not absorb bromine at all upon reaction with alcoholic bromine.

Upon boiling the non-brominable isomers in alcohol or benzene, their transformation into brominable isomers occurs, which quantity reaches defined limits, corresponding to the above-mentioned percentage contents. These limits are practically obtained within 1 hour. For example, upon boiling the non-brominable isomer of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine in alcohol or benzene, within 10 minutes the contents of brominable isomer reaches 10-11%, after 30 minutes of boiling —16-17%, after 1 hr of boiling —18-21%. Further boiling does not change the ratio of brominable and non-brominable isomers in the mixture. Boiling of the non-brominable isomers in glacial acetic acid results in higher bromometrical analysis results, which is explained by partial acetylation (see below).

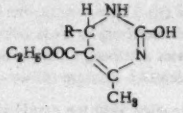
The attainment of one and the same constant limit every time indicates that the observed isomerization of the non-brominable isomer into the brominable represents a reversible process. In boiling alcohol or benzene it proceeds at a measurable rate: the equilibrium point is reached in approximately 1 hr. At 0°, and even at 17°, this rate is so much less that the non-brominable isomers can be successfully separated and can be obtained practically free of the brominable. The reverse process proceeds at a high rate, because in the equilibrium mixture the non-brominable isomers are present in large amount.

The tautomeric transformation consists of migration of the hydrogen atom on carbon 5 to one of the heteroatoms (position 1 or 3), and conversely, with corresponding replacement of the double bonds in the ring.

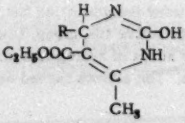
This tautomerism (desmotropism) explains the ability of the investigated dihydropyrimidines to enter into azo combination reaction at the expense of the hydrogens of the methyl group, and also their ability to add bromine at the double bond. Thus the unusual difficulty of bromination and the necessity for conducting bromination at elevated temperature is clarified.



5,6-dihydropyrimidine

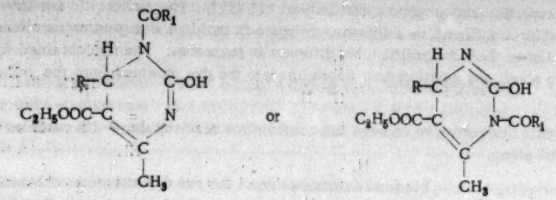


1,6-dihydropyrimidine



3,6-dihydropyrimidine

Examination of the structural formulas of 1,6- or 3,6-dihydropyrimidine derivatives leads to the conclusion that these compounds should be capable of acetylation, similar to dihydrouracil [12], with the formation of 1- or 3-acyl derivatives.

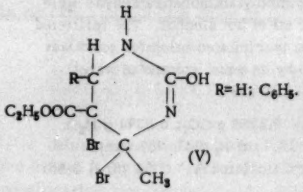


These N-acyl derivatives, no longer being capable of transformation into 5,6-dihydropyrimidine compounds, should easily brominate 100% in the cold, like ethylenic compounds, and at the same time their methyl group should not be reactive.

Experiment fully confirmed these theoretical assumptions. N-acetyl-2-hydroxy-4-methyl-5-carbethoxy-dihydropyrimidine and N-acetyl-2-hydroxy-4-methyl-5-carbethoxy-6-phenyl-dihydropyrimidine, synthesized by the authors, brominated quantitatively under conditions of the above-described bromometrical titration, but did not conjugate with p-nitrodiazobenzene.

Acetylation was effected with acetic anhydride; however, partial acetylation already occurred upon boiling in glacial acetic acid. This explains why boiling the non-brominable tautomers in glacial acetic acid gave above-normal results at the time of bromometric analysis of the produced mixture of tautomers (see above).

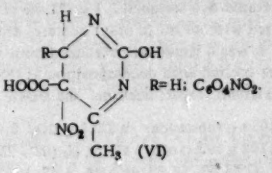
The authors also subjected dibromoderivatives of the investigated dihydropyrimidines to the reaction of diazo combination. The structure of these dibromides is such (V) that displacement of the double bond in position 3-4 is impossible; thus, activation of the methyl group is also impossible. Practice has shown that they are incapable of undergoing azo combination with p-nitrodiazobenzene.



The authors have expressed above an assumption that the investigated dihydropyrimidines enter into azo combination reaction at the expense of the hydrogens of the active methyl group. However, the tautomerism phenomenon detected by the authors points to mobility of the hydrogen atom in position 5. Thus it could be assumed that at the time of azo combination this atom of hydrogen is replaced by the rest of the diazo compound. If such a hypothesis could not emerge from the interaction with p-dimethylaminobenzaldehyde, because two hydrogen atoms situated at one carbon atom are split during this condensation, then during the azo combination reaction such an assumption can develop, since only one hydrogen atom is necessary for monoazo dye formation. In order to eliminate such an assumption, the authors substituted the hydrogen atom in position 5 by a nitro group.

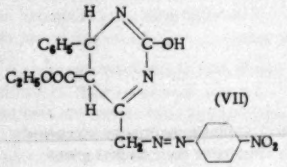
It was found that during reaction of the nitrated mixture with the investigated dihydropyrimidines, there simultaneously occurred nitration and saponification of the carbethoxyl group.

The obtained 2-hydroxy-4-methyl-5-nitrodihydropyrimidine-5-carboxylic acid[(VI), R= H; silky-white needles, m.p. 142.5-143.5°] in pyridine conjugates with p-nitrodiazobenzene. Upon nitration of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine there is formed 2-hydroxy-4-methyl-5-nitro-6-p-nitrophenyldihydropyrimidine-5-carboxylic acid (VI, R= $C_6H_4NO_2$-p). The position of the nitro group in the phenyl radical was determined by means of



oxidation, as the result of which there is formed p-nitrobenzoic acid. The obtained dinitro compound — a white crystalline substance (m.p. 133.5-134.5°) — was soluble in alkali and in carbonates with yellow coloration. Upon acidification of the solution there precipitated a bright-yellow substance of the same composition as the white one, but possessing different properties (decomposed explosively at 117-118°). The authors did not investigate this transformation. Both the white and the yellow substance conjugate in pyridine with p-nitrodiazobenzene. Thus are formed monoazo dyes, similar in their composition, but different in properties. The dye obtained from the white substance, upon solution in alkali and acidification, transforms into the dye obtained from the yellow substance.

The ability of the obtained nitro derivatives to undergo azo combination reaction shows this reaction proceeds at the expense of the methyl group.



(VII)

For final determination of the azo dye structures obtained from dihydropyrimidines, 2-hydroxy-4-nitrobenzeneazomethyl-5-carbethoxy-6-phenyldihydropyrimidine was subjected to the action of bromine in chloroform while heating. The test showed that this dye is unable to take up bromine. Consequently, it could be assumed to represent the 5,6-dihydropyrimidine derivative (VII).

EXPERIMENTAL

Synthesis of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine [3-5]. 6 g of urea, 10.6 g of benzaldehyde, 19.5 g of acetoacetic ester, 40 ml of alcohol and 16 drops of concentrated hydrochloric acid were refluxed for three hours. After cooling, the precipitate was filtered off, washed with alcohol and dried. Yield 23.75 g (84.5% of theoretical). After 4 recrystallizations from alcohol, m.p. 206-207°.

Synthesis of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine [5]. 23.1 g of methyleneurea [13], 53.5 g of acetoacetic ester, 150 ml of glacial acetic acid and 20 drops of concentrated hydrochloric acid were refluxed for 5 hours and then put aside to stand for 14-16 hours. The light yellow precipitate formed was filtered off, washed with a small quantity of aqueous alcohol, and dried. Yield 16.5-18 g (20-22% of theoretical). After a single recrystallization from alcohol the m.p. was 254-256°.

Condensation of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine with p-dimethylaminobenzaldehyde. 1.84 g of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine and 1.49 g of p-dimethylaminobenzaldehyde were melted together for 3 hrs at 205-210°. The cooled cake was extracted with 30 ml of hot alcohol. The reiltered red solution was poured, while mixing, into 10 times its volume of water. The precipitated brick-red solid was purified by dissolution in 30 volumes of alcohol, with subsequent precipitation by an equal volume of water. The substance was soluble in alcohol, acetone, benzene, and chloroform; m.p. 194-198°.

0.0690 g substance: 0.1636 g CO_2; 0.0411 g H_2O. 0.1008 g substance: 0.2382 g CO_2; 0.0574 g H_2O. 0.0908 g substance: 10.5 ml N_2 (24°, 767 mm). 0.1106 g substance: 12.7 ml N_2 (24°, 767 mm). Found %: C 64.66, 64.42; H 6.54, 6.38; N 13.24; 13.16. $C_{17}H_{21}O_3N_3$. Calculated %: C 64.76; H 6.66; N 13.33.

Interaction of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine with 1 mole of p-nitrodiazobenzene. To the cooled solution of 2.6 g of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine and 4 g of anhydrous sodium acetate in 50 ml of glacial acetic acid was added, with mixing, a solution of p-nitrodiazobenzene, prepared from 1.38 g of p-nitraniline, 3.7 ml of concentrated hydrochloric acid, 2.2 ml of water and 0.7 g sodium nitrite dissolved in 2.1 ml of water. The reaction mixture was stirred for 3 hours and put aside for 14-16 hours at room temperature. The filtered solution was diluted with 6 times its volume of water. The precipitated dye weighed 3.1 g (71.4% of the theoretical). For purification, the dye was boiled with water and extracted with 40 ml of ethyl acetate, after evaporation of which there remained a glittering, dark-red sediment. It was 4 times recrystallized from alcohol (40 volumes), which resulted in considerable loss. The purified dye melted with decomposition at 155-157°; with alcoholic alkali a bright violet color resulted. Readily soluble in alcohol, ether, acetone, and acetic acid; less so in benzene and toluene.

0.1033 g substance: 0.2218 g CO_2; 0.0456 g H_2O. 0.1202 g substance: 0.2584 g CO_2; 0.0501 g H_2O. 0.1133 g substance: 17 ml N_2 (22°, 754 mm). 0.1022 g substance: 15.5 ml N_2 (20°, 750 mm). Found %: C 58.58, 58.63; H 4.98, 4.67; N 17.1, 17.3. $C_{20}H_{19}O_5N_5$. Calculated %: C 58.68; H 4.64; N 17.11.

Interaction of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine with 2 moles of p-nitrodiazobenzene. Procedure as in the previous case; there was taken only double the volume of sodium acetate and diazo solution and 60 ml of glacial acetic acid. After 48 hours 2.1 g of the dye (52.5% of theoretical) was filtered off. It was purified by repeated recrystallization from alcohol (1:35) or from glacial acetic acid (1:10) with the addition of a small volume of water. The dye melted with decomposition at 175-177°; with alcoholic alkali it gave a sky-blue coloration.

0.1102 g substance: 0.2342 g CO_2; 0.0398 g H_2O. 0.1054 g substance: 0.2261 g CO_2; 0.0390 g H_2O. 0.0995 g substance: 15.1 ml N_2 (20°, 750 mm). 0.0875 g substance: 13.2 ml N_2 (21°, 757 mm). Found %: C 58.45, 58.52; H 4.03, 4.15; N 17.3, 17.27. $C_{20}H_{17}O_5N_5$. Calculated %: C 58.69; H 4.1, N 17.12.

The same compound is obtained upon reaction of 1 mole p-nitrodiazobenzene with the azo dye obtained in the preceding instance.

Interaction of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine with p-sulfamidodiazobenzene. To the cooled solution of 2.6 g of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine and 5 g of anhydrous sodium acetate in 50 ml of glacial acetic acid was added a solution of p-sulfamidodiazobenzene, prepared from 1.72 g of sulfanilamide (dissolved in a mixture of 5.5 ml of concentrated hydrochloric acid and 7 ml of water) and 0.7 g of sodium nitrite (in the form of 25% solution). The mixture was stirred for 2-3 hours and left at room temperature for 14-16 hrs. The dark red solution was filtered, diluted with 4 times the volume of water, and the precipitate separated, washed with water, and dried at 50-60°. Yield 3.7 g (75.8% of theory). To purify, the precipitate was boiled with water, after drying extracted by cold acetone and the acetone driven off, crystallized from alcohol (1:25) or from 50% acetic acid (1:20). M.p. above 240°. Gave raspberry-red color with alcoholic alkali.

0.0952 g substance: 0.1882 g CO_2; 0.0391 g H_2O. 0.0804 g substance: 0.1592 g CO_2; 0.0342 g H_2O. 0.1210 g substance: 16.5 ml N_2 (20°, 757 mm). 0.0905 g substance: 12.7 ml N_2 (20°, 750 mm). Found %: C 53.92, 54.02; H 4.59, 4.76; N 15.63, 15.91. $C_{20}H_{21}O_5N_5S$. Calculated %: C 54.17; H 4.74; N 15.8.

Interaction of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine with p-nitrodiazobenzene. Azo-conjugation of 1.84 g of the initial substance was conducted at 0° in the manner described above for the phenyl analog. Yield 2.8 g (87.4% of theoretical). After purification with boiling water and extraction by ethyl acetate the product was recrystallized 3 times from alcohol (1:25) or from 70% acetic acid (1:15). From the alcoholic alkali the substance gave a blue color; m.p. 174-176°.

0.1020 g substance: 0.1883 g CO_2; 0.0428 g H_2O. 0.1104 g substance: 0.2033 g CO_2; 0.0441 g H_2O. 0.0910 g substance: 16.6 ml N_2 (21°, 763 mm). 0.1203 g substance: 21.7 ml N_2 (20°, 763 mm). Found %: C 50.34, 50.23; H 4.69, 4.47; N 21.06, 20.88. $C_{14}H_{15}O_5N_5$. Calculated %: C 50.45; H 4.5; N 21.02.

When this azo conjugation was conducted in 70 ml of glacial acetic acid and diazo solution, there was then formed 2.7 g (81% of theoretical) of brown azo dye. It was purified by extraction with cold acetone and crystallization from alcohol (1:15). It melted with decomposition at 185-187°; in alcoholic alkali it gave a dark-violet color.

0.1034 g substance: 0.1920 g CO_2; 0.0358 g H_2O 0.1074 g substance: 0.1991 g CO_2; 0.0386 g H_2O. 0.1416 g substance: 26.1 ml N_2 (22°, 760 mm). 0.1306 g substance: 24.8 ml N_2 (24°, 757 mm). Found %: C 50.65, 50.47; H 3.87, 4.02; N 21.03, 21.32. $C_{14}H_{13}O_5N_5$. Calculated %: C 50.75; H 3.92; N 21.14.

Interaction of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine with p-sulfamidodiazobenzene. 1.84 g of the initial substance and 5 g of anhydrous sodium acetate were dissolved in 60 ml of glacial acetic acid. At 0° the diazo solution prepared from 1.72 g of sulfanilamide was poured in. The reaction mixture was left to stand on ice for 14-16 hours. The dye was isolated by dilution of the filtered solution with water. Yield 2.9 g (79.6% of theoretical). The dye was purified as described above for the phenyl analog. The dye melted indefinitely above 260°; with alcoholic alkali it gave color.

0.0891 g substance: 0.1488 g CO_2; 0.0385 g H_2O. 0.1031 g substance: 0.1726 g CO_2; 0.0425 g H_2O. 0.0932 g substance: 15.5 ml N_2 (21°, 763 mm). 0.0972 g substance: 16.4 ml N_2 (20°, 757 mm). Found %: C 45.5, 45.66; H 4.78, 4.38; N 19.20, 19.31. $C_{20}H_{21}O_5N_5S$. Calculated %: C 45.77; H 4.63; N 19.13.

Bromination of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine [4,11]. To the exact weight of 2.6 g of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine suspended in 20 ml of chloroform was added a solution of 1.37 ml of bromine in 40 ml of chloroform. The mixture was stirred for 40 minutes at room temperature, and then for 30 minutes at boiling. The chloroform was driven off to a volume of 10 ml, and 25 ml of alcohol added, and the remaining chloroform distilled off with it. After cooling, the precipitate was filtered off and dried. Yield 3.5 g (83% of theoretical), m.p. 182-183° (with decomposition). The dibromide was purified by recrystallization from alcohol.

Bromination of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine. The initial substance (5.4 g) was suspended in 60 ml of chloroform, and 4.2 ml of bromine in 150 ml of chloroform added. The mixture was stirred for 20 minutes at room temperature, and then for 1 hour while boiling. The chloroform was driven off in vacuo to a volume of 10-15 ml, 30 ml of alcohol added, and distilled off again in vacuo to a volume of 10 ml. The remainder was left for 24 hrs in vacuo; the precipitate was then filtered off, washed with aqueous alcohol and dried in vacuo. Yield 7.28 g (70.6% of theoretical). The dibromide was recrystallized from 30% alcohol (1:5). It appeared as white, large crystals, soluble in alcohol, acetone, chloroform and acetic acid; m.p. 115-116° (with decomposition).

0.0892 g substance: 0.0915 g CO_2; 0.0284 g H_2O. 0.0918 g substance: 0.0948 g CO_2; 0.0291 g H_2O. 0.0964 g substance: 7.1 ml N_2 (20°, 748 mm). 0.1174 g substance: 8.4 ml N_2 (21°, 768 mm). Found %: C 27.99, 28.01; H 3.57, 3.61; N 8.38, 8.3. $C_9H_{12}O_3N_2Br_2$. Calculated %: C 27.9; H 3.48; N 8.14.

For debromination, the obtained dibromides were dissolved in alcohol (30 parts), 4 parts of zinc dust added, and boiled for 7 hours while stirring. The hot solution was filtered and the filtrate diluted with water. After a time the crystals of initial dihydropyrimidine precipitated.

Determination of the percentage of brominated isomers in the investigated dihydropyrimidines. The determination was carried out on the substances three times recrystallized from alcohol. The weighed portion of substance was dissolved in alcohol and an excess of freshly prepared, titrated, alcoholic bromine solution (approximately 10-12%) added. After a given bromination time an excess of potassium iodide was added as a 50% aqueous solution. The separated iodine was titrated by 0.1 N hyposulfite solution in the presence of starch. The determination was conducted twice in each case.

The percentage contents of brominated isomers (C) was calculated according to the following formula:

$$C = \frac{(a-b)\cdot M\cdot 100}{c\cdot 20000}$$

where a = number of ml of 0.1 N hyposulfite solution used for titration of the alcoholic bromine solution used; b = the number of ml of 0.1 N hyposulfite solution used for titration of the excess bromine remaining after bromination of the weighed portion of substance; c = weighed sample of analyzed substance; M = molecular weight of the analyzed substance.

Results of the determination are summarized in Tables 1 and 2.

Separation of the nonbrominable isomers. Rate of equilibrium attainment. The reaction mixture left after bromometric titration was diluted with double the volume of water. The nonbrominable isomer precipitated. The precipitate was washed with water and cold alcohol, and dried at room temperature. The dihydropyrimidines thus obtained did not completely absorb bromine upon treatment with the titrated solution of alcoholic bromine. Upon their boiling in a solution of alcohol or benzene the percentage contents of brominable isomers increased, and after 1 hour of boiling reached the equilibrium values given in Tables 1 and 2.

Derivation of N-acetyl-2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine. Its titration. 5.2 g of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine and 50 ml of acetic anhydride were boiled for 3 hours with a reflux condenser. The cooled solution was gradually diluted with 5 times its volume of water. The precipitated substance weighed 4.1 g (68.3% of theoretical). It was difficultly soluble in water, readily soluble in acetic acid, acetone, and hot alcohol (1:6), from which it crystallized in the form of light, white flakes; m.p. 176-177°.

0.1014 g substance: 0.2359 g CO_2; 0.0541 g H_2O. 0.0824 g substance: 0.1928 g CO_2; 0.0440 g H_2O. 0.1525 g substance: 12.4 ml N_2 (23°, 759 mm). 0.1220 g substance: 10.1 ml N_2 (22.5°, 768 mm). Found %: C 63.47, 63.84; H 6.0, 5.98; N 9.29, 9.46. $C_{16}H_{18}O_4N_2$. Calculated %: C 63.6, H 5.96; N 9.27.

TABLE 1

2-Hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine

Test No.	Temp. (in °C)	Duration of bromination (in minutes)	c (g)	a (ml)	b (ml)	M	C (in %)
1	0	5	0.2	23.5	20.5	260	19.5
2	0	5	0.2	24.4	20.5	260	18.85
3	0	15	0.2	23.6	20.6	260	19.5
4	0	15	0.2	23.5	20.4	260	20.15
5	17	5	0.2	27.45	24.3	260	20.47
6	17	5	0.2	27.5	24.4	260	20.15
7	17	15	0.2	27.6	24.5	260	20.15
8	17	15	0.2	27.8	24.6	260	20.8

TABLE 2

2-Hydroxy-4-methyl-5-carbethoxydihydropyrimidine

Test No.	Temp. (in °C)	Duration of bromination (in minutes)	c (g)	a (ml)	b (ml)	M	C (in %)
1	0	5	0.25	25.8	24.1	184	6.25
2	0	5	0.25	25.7	23.9	184	6.62
3	0	15	0.25	25.6	23.9	184	6.25
4	0	15	0.25	25.7	24.1	184	5.7
5	17	5	0.25	25.5	23.7	184	6.62
6	17	5	0.25	25.6	23.9	184	6.25
7	17	15	0.25	25.6	23.8	184	6.62
8	17	15	0.25	25.4	23.5	184	6.99

TABLE 3

N-Acetyl-2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine

Test No.	Temp. (in °C)	Duration of bromination (in minutes)	c (g)	a (ml)	b (ml)	M	C (in %)
1	0	5	0.25	28.6	12.4	302	97.9
2	0	5	0.25	28.8	12.5	302	98.5
3	0	15	0.25	28.6	12.2	302	99.1
4	0	15	0.25	28.5	12.3	302	97.9
5	17	5	0.25	28.7	12.4	302	98.5
6	17	5	0.25	28.5	12.1	302	99.1
7	17	15	0.25	28.4	11.9	302	99.7
8	17	15	0.25	28.2	11.7	302	99.7

Results of the bromometric determination of the obtained substance are summarized in Table 3.

Derivation of N-acetyl-2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine. Its titration. 3.68 g of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine and 36 ml of acetic anhydride were boiled for 3 hours with a reflux. After cooling the solution and diluting it with 7 times its volume of water, there was precipitated 2.8 g (61.9% of theoretical) of the solid. Crystallized from alcohol (1:20), water (1:100) or 50% acetic acid (1:10) in the form of long white needles (by slow cooling); m.p. 149.5-150.5°.

0.1187 g substance: 0.2304 g CO_2; 0.0651 g H_2O. 0.0802 g substance: 0.1562 g CO_2; 0.0442 g H_2O. 0.1274 g substance: 13.5 ml N_2 (24°, 760 mm). 0.1062 g substance: 11.4 ml N_2 (22°, 758 mm). Found %: C 52.9, 53.14; H 6.14, 6.17; N 12.03, 12.24. $C_{16}H_{14}O_4N_2$. Calculated %: C 53.09; H 6.19; N 11.9.

The dibromide of the given compound reacts in the cold with potassium iodide, separating iodine. Thus, upon titration, the excess of bromine was bound with β-naphthol [14,15], after which there was added a solution of potassium iodide, and after 4 hours the separated iodine was titrated with 0.1 N hyposulfite solution.

During titration of the 0.2 g weighed sample, after 5 minutes of bromination 17.6 ml of hyposulfite was consumed, from which $C = \frac{17.6 \cdot 226 \cdot 100}{0.2 \cdot 20000} = 99.44\%$ (226 - molecular weight). After 15 minutes of bromination there was consumed 17.7 ml of the hyposulfite solution, from which $C = \frac{17.7 \cdot 226 \cdot 100}{0.2 \cdot 20000} = 100.01\%$.

The obtained N-acetyl derivatives, and also the dibromoderivatives of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine and of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine, were subjected to reaction with p-nitrodiazobenzene under the above-described conditions. In no case was azo conjugation observed; the initial substances were recovered unchanged.

Nitration of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine. 3.68 g of the initial substance was dissolved in 22 ml of concentrated sulfuric acid, 22 ml of 10% potassium nitrate solution in concentrated sulfuric acid was added, and the mixture obtained was allowed to stand for 4 hours at 40-45°. After cooling, the solution was poured into an equal volume of water, and the precipitated white product was filtered off, washed with water and dried at 50-55°. Yield 3.6 g (90% of theoretical). The nitrocarboxylic acid obtained was recrystallized from water (1:100), alcohol (1:10) or from 50% acetic acid (1:6). Long silky needles, soluble in alkali, carbonates and pyridine, with a yellow coloration. M.p. 142.5-143.5°. The salts of lead, copper, nickel and cobalt were hard to dissolve.

0.0940 g substance: 0.1235 g CO_2; 0.0371 g H_2O. 0.1039 g substance: 0.1361 g CO_2; 0.0340 g H_2O. 0.0810 g substance: 14.5 ml N_2 (20°, 763 mm). 0.0932 g substance: 17.2 ml N_2 (22°, 748 mm). Found %: C 35.83, 35.70; H 3.67, 3.66; N 20.74, 20.79. $C_8H_7O_5N_3$. Calculated %: C 35.82; H 3.48; N 20.89.

The substance was also able to conjugate in pyridine solution with p-nitrobenzene. Upon pouring the raspberry-red pyridine solution into diluted hydrochloric acid, the precipitate of brown azo dye separated.

Nitration of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine. To 5.2 g of the initial substance in 30 ml of concentrated sulfuric acid was added dropwise, with stirring, 30 ml of a 10% solution of potassium nitrate in concentrated sulfuric acid. After 1 hour the reaction liquid was poured into 15 times its volume of water. The precipitated white product was filtered off, washed with water, and dried in vacuo. Yield 6.41 g (99.5% of theoretical). After three recrystallizations from 50% acetic acid (1:20) its m.p. was 133.5-134.5°. The substance dissolved in alcohol, ether, and acetone. Soluble in alkali and carbonates with yellow coloration.

0.0812 g substance: 0.1334 g CO_2; 0.0241 g H_2O. 0.1025 g substance: 0.1675 g CO_2; 0.0301 g H_2O. 0.1034 g substance: 15.8 ml N_2 (21°, 766 mm). 0.1082 g substance: 16.8 ml N_2 (21°, 752 mm). Found %: C 44.81, 44.55; H 3.32, 3.28; N 17.57, 17.65. $C_{12}H_{10}O_7N_4$. Calculated %: C 44.72; H 3.13; N 17.39.

For transformation into the yellow isomer the obtained substance was dissolved in 0.1 N alkali, and a 1 N solution of hydrochloric acid was added dropwise at 0°. The yellow substance obtained, without melting, decomposed with a flash at 117-118°; soluble in alcohol, acetone, acetic acid, pyridine, aqueous alkali, and carbonates.

0.0812 g substance: 0.1325 g CO_2; 0.0222 g H_2O. 0.0817 g substance: 0.1336 g CO_2; 0.0232 g H_2O. 0.0988 g substance: 15.2 ml N_2 (22°, 755 mm). 0.1117 g substance: 17.4 ml N_2 (21°, 753 mm). Found %: C 44.5, 44.59; H 3.06, 3.17; N 17.49, 17.68. $C_{12}H_{10}O_7N_4$. Calculated %: C 44.72; H 3.13; N 17.39.

Oxidation of 2-hydroxy-4-methyl-5-nitro-5-carboxy-6-nitrophenyldihydropyrimidine. 3.22 g (0.01 mole) of 2-hydroxy-4-methyl-5-nitro-5-carboxy-6-nitrophenyldihydropyrimidine was dissolved in 100 ml of 5% potassium hydroxide solution. To the solution was gradually added, with heating, 12 g of potassium permanganate, and the mixture was then boiled for one hour and a half with a reflux. The colored solution was decolorized by a small volume of alcohol. The precipitate of manganese dioxide was filtered off and the colorless solution steamed off on a water bath to a volume of 50-60 ml, and acidified to Congo red with 5% hydrochloric acid. Immediately a slightly yellow precipitate separated. After washing with water and drying, the precipitate melted at 235-236°, and after a single crystallization at 238°. A mixture of the precipitate with an authentic sample of p-nitrobenzoic acid also melted at 238°. Thus it can be deduced that the initial compound has the structure (VI) (R = $p\text{-}O_2NC_6H_4^-$).

Interaction of 2-hydroxy-4-methyl-5-nitro-6-nitrophenyldihydropyrimidine-5-carboxylic acid with p-nitrodiazobenzene. 6.44 g of the dinitro acid (both white and yellow) was dissolved in 40 ml of pyridine and to the solution was added 1 mole of p-nitrodiazobenzene. The solution immediately turned dark-red. After 2 hrs it was poured in 700 ml of 5% hydrochloric acid. The bright red azo dye obtained from the white dinitro acid, was crystallized 3 times from 1.5% alcoholic hydrochloric acid (1:12). M.p. 173-175°. Soluble in alcohol, acetone, pyridine, and acetic acid. In alcoholic alkali its color becomes dark-red.

0.0835 g substance: 0.1406 g CO_2; 0.0191 g H_2O. 0.1086 g substance: 0.1816 g CO_2; 0.0273 g H_2O. 0.1012 g substance: 18.5 ml N_2 (22°, 755 mm). 0.0930 g substance: 17.1 ml N_2 (23°, 753 mm). Found %: C 45.83, 45.61; H 2.52, 2.81; N 20.81, 20.75. $C_{18}H_{13}O_9N_7$. Calculated %: C 45.86; H 2.76; N 20.8.

The brown dye, obtained from the yellow dinitroacid, was purified by crystallization from 1.5% alcoholic hydrochloric acid (1:125). M.p. 204-206°. In alcoholic alkali, it gave the same coloration as the preceding dye.

0.1106 g substance: 0.1868 g CO_2; 0.0260 g H_2O. 0.1023 g substance: 0.1712 g CO_2; 0.0242 g H_2O. 0.0801 g substance: 14.5 ml N_2 (21°, 763 mm). 0.0906 g substance: 16.5 ml N_2 (21°, 763 mm). Found %: C 46.12, 45.66; H 2.63, 2.65; N 20.91, 21.03. $C_{18}H_{13}O_9N_7$. Calculated %: C 45.86; H 2.76; N 20.8.

The dye obtained from the white dinitroacid, after dissolution in alkali and subsequent acidification, transformed into the dye obtained from the yellow dinitroacid.

Reaction of bromine with 2-hydroxy-4-p-nitrobenzeneazomethyl-5-carbethoxy-6-phenyldihydropyrimidine. 2.1 g of the dye was dissolved in 60 ml of dry chloroform and 2.4 g of bromine, dissolved in chloroform was added. After prolonged boiling, the chloroform was distilled off and 60 ml of alcohol was added. Upon cooling, from the solution separated the initial dye, not containing bromine; its mixture with the initial dye gave no depression of melting point.

SUMMARY

1. The activity of the methyl group in six-membered heterocycles, containing two double bonds in the ring, was studied, namely, in the monohydroxydihydropyrimidines. It was shown that the methyl group in the investigated compounds possesses high activity, sufficient for condensation with aldehydes and diazo compounds.

2. It was demonstrated that the dihydropyrimidines, obtained by the Biginelli condensation, are represented as an equilibrium mixture of tautomers, the relative quantity of which is determined by the bromometric method.

3. The structural formula proposed by Biginelli for the dihydropyrimidines does not conform to the displayed activity of the methyl group.

4. Tautomers incapable of bromination were isolated in the free state. Upon boiling in alcohol, benzene, or glacial acetic acid, they are again transformed into an equilibrium mixture of tautomers with constant composition.

5. The derivation of N-acetyl derivatives, their ability to combine with bromine, and their inability to conjugate with diazo compounds confirm that the active methyl group exists in only one definite tautomeric form of the dihydropyrimidines. The proposed structural formula for this tautomer explains the observed activity of the methyl group in the investigated dihydropyrimidines.

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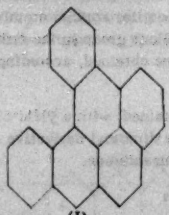
THE SYNTHESIS OF 3,4-BENZOPYRENE AND 3,4,6,7-DIBENZOPYRENE FROM PHENALONE-9 AND BENZANTHRONE*

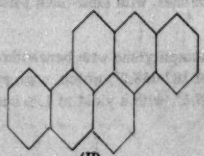
B. A. Arbuzov and N. P. Grechkin

One of the most actively investigated carcinogenic substances is 3,4-benzopyrene, to which more than 200 works had been devoted by 1941. As regards the hexa-nuclear hydrocarbons and the hydrocarbons with a large number of condensed nuclei, much less material exists.

In the period 1935-1941 there were synthesized and investigated for carcinogenic activity some dibenzopyrenes and naphthobenzopyrenes. 1,2,3,4-Dibenzopyrene (I) [1] and 3,4,8,9-dibenzopyrene (II) [2]** showed considerable carcinogenicity, while at the same time 2', 3'-naphtho-3,4-pyrene (III) proved to be inactive [3].



(I)



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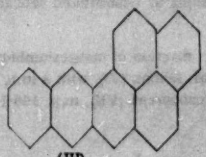
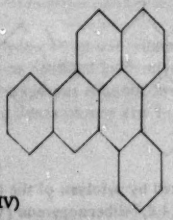


(III)

In 1941, A. E. Arbuzov and N. P. Grechkin [4] synthesized 3,4,6,7-dibenzopyrene (IV) and 1', 2', 3', 4'-naphtho-6,7-benzopyrene (V) for the purpose of explaining the influence of structure upon carcinogenicity of hexa-nuclear hydrocarbons, and the possibility for carcinogenicity of hepta-nuclear compounds.



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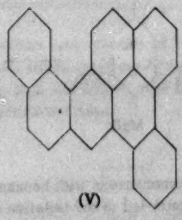


(V)

The war temporarily interrupted the investigations, both in the synthesis of the polynuclear hydrocarbons and in the testing of their carcinogenicity, in favor of training physicians, conducted by N. I. Vylegzhanin at the Kazan State Institute. After termination of the war, these researches were resumed and interesting data were soon obtained. At the present time it is possible to consider as fully proven the high blastomogenic activity of both hydrocarbons. Tests conducted by N. I. Vylegzhanin on white mice have demonstrated the very high blastomogenic activity of 3,4,6,7-dibenzopyrene, forming both sarcomas and cancerous tumors. On the basis

* Results reported during the session of the Division of Chemical Sciences, Academy of Sciences, USSR and Academy of Sciences of the Ukraine, USSR, in Kiev, June 1950; see the Annals of the Academy of Sciences, Division of Chemical Sciences 552 (1950).

** Evidently the same hydrocarbon, under the name of 1,2,6,7-dibenzopyrene, was investigated by Voronyansky, Pisareva and Sorin [10], because Zilberman [9], having synthesized this hydrocarbon, gave it the formula (II), although the m.p. of Zilberman's sample was higher by 17° than that of hydrocarbon (II).

of N. I. Vylegzhanin's data, 3,4,6,7-dibenzopyrene can be placed in the same group with such strong blastomogenic substances as 3,4-benzopyrene and 20-methylcholanthrene. It should be noted that 3,4,6,7-dibenzopyrene was found to be non-toxic for white mice, which facilitates work with it.

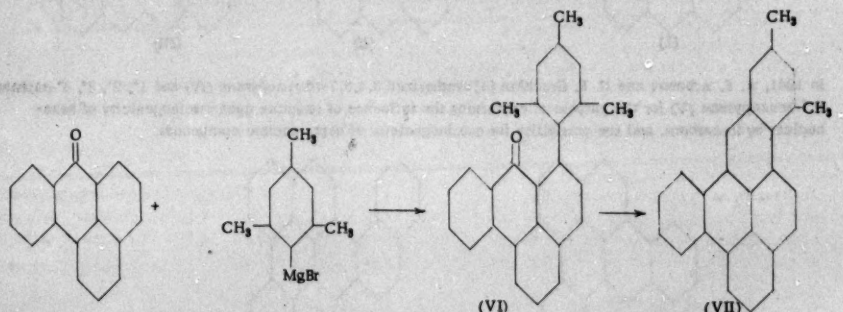
Within two years after publication of the article on the synthesis of 3,4,6,7-dibenzopyrene, Clar [5] described its synthesis by an entirely different, more complicated method, starting with 1,2,3,4,5,6,7,8-octahydroanthracene, through the 10-benzoyl derivative. The Clar synthesis is complex and accompanied by isomerizations, and along with 3,4,6,7-dibenzopyrene there is obtained 1,2,6,7-dibenzopyrene, which is separated by recrystallization of the picrates. The melting point of Clar's 3,4,6,7-dibenzopyrene is 14° lower, which can be explained either by insufficient purity of the Clar sample, or by a different method of melting point determination. Clar makes no reference to carcinogenicity test data.

No less interesting data were obtained by N. I. Vylegzhanin with 1', 2', 3,4-naphtho-6,7-benzopyrene, containing 7 nuclei. The hydrocarbon was found to be blastomogenic, inducing the appearance of sarcomas and leukemia.

The data cited on the blastomogenic action of 3,4,6,7-dibenzopyrene and 1', 2', 3,4-naphtho-6,7-benzopyrene stimulated the authors to continue the work on synthesis of various polynuclear hydrocarbons of the 3,4,6,7-dibenzopyrene type. Certain of the obtained results are reported in the present article.

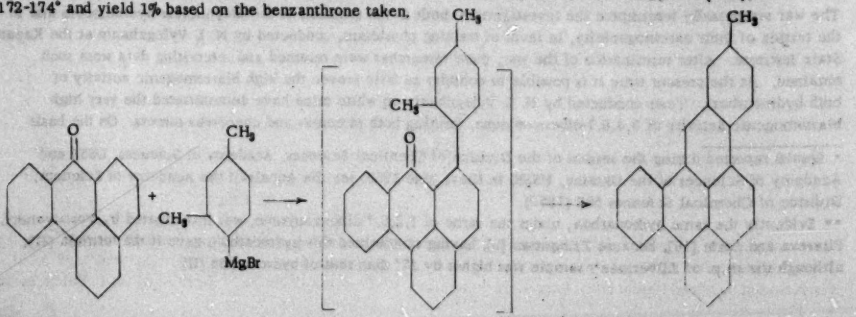
For the synthesis of derivatives of 3,4,6,7-dibenzopyrene, the authors used the earlier applied method of reaction of arylmagnesium halide with benzanthrone, containing a methyl or methylene group in the ortho position, leading to 4-substituted benzanthrones, with subsequent pyrolysis of the ketone obtained, according to Elbs.

Upon reaction of mangesiumbromomesitylene with benzanthrone there was obtained, with a yield 59% of theoretical, ketone (VI), with a m.p. of 167-168.5°, which, upon pyrolysis, gave the dimethyl derivative of 3,4,6,7-dibenzopyrene (VII), m.p. 166-167.5°, with a yield of 11% based on mesitylbenzanthrone.



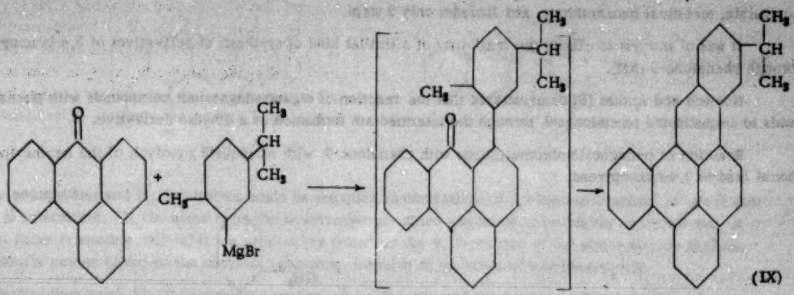
(VI) (VII)

Reaction of 1,3-dimethyl-4-magnesiumbromobenzene with benzanthrone, followed by pyrolysis of the ketone, which could not be isolated in the free state, led to the isolation of 3-methyl-3,4,6,7-dibenzopyrene (VIII), m.p. 172-174° and yield 1% based on the benzanthrone taken.



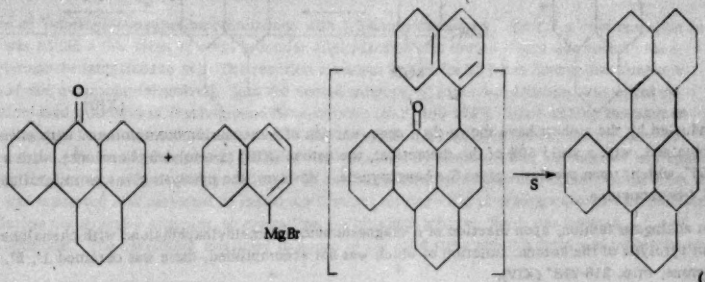
(VIII)

By a similar procedure, upon reaction of 2-mangesiumbromocymene with benzanthrone there was obtained the isopropyl derivative of 3,4,6,7-dibenzopyrene (IX), m.p. 124.5-126.5°. Cymylbenzanthrone could not be separated in the pure state, and the crude reaction product was pyrolized.



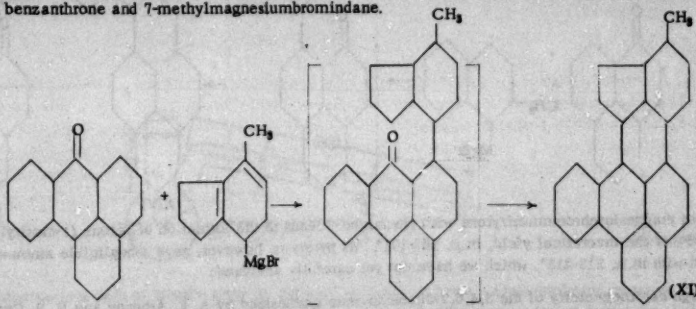
(IX)

Upon reaction of α-magnesiumbromotetraline with benzanthrone there was obtained a hard noncrystalline product. Its pyrolysis, with subsequent dehydration by sulfur, led to isolation of an insignificant yield (3%) of 3,4,5,6,7-tribenzopyrene (X) with m.p. 206-207°.



(X)

An interesting hydrocarbon was synthesized by the authors upon reaction of 7-methyl-4-magnesiumbromindane with benzanthrone followed by pyrolysis of the ketone, which could not be isolated in the pure state. As a result of the pyrolysis there was obtained hydrocarbon (XI), m.p. 241-242.5°, with a 12% yield for the raw reaction product between benzanthrone and 7-methylmagnesiumbromindane.



(XI)

Hydrocarbon (XI) (3'-methyl-4',5-ethylene-3,4,6,7-dibenzopyrene) is of particular interest since it contains within itself the framework of some of the strongest carcinogens: 3,4-benzopyrene, 20-methylcholanthrene and 9,10-disubstituted 1,2-benzanthracene. Experiments testing its blastomogenic action, conducted by N. I. Vylegzhanin,

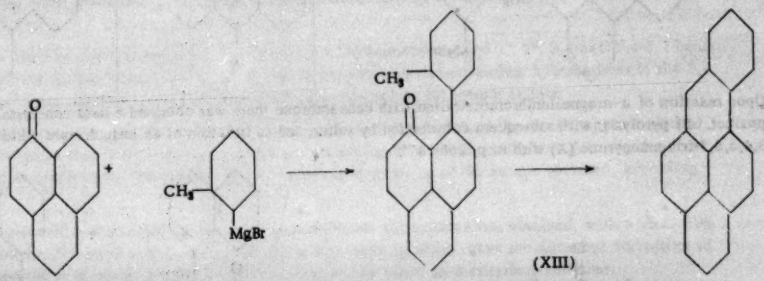
have shown that it possesses weak blastomogenic, but intense frank leukemic, action.

Syntheses of the polynuclear hydrocarbons are found, as a rule, to be multistage. The method applied by the authors, using benzanthrone, though it gives small yields of final products, is based upon the utilization of accessible, technical benzanthrone, and includes only 2 steps.

It was of interest to clarify the feasibility of a similar kind of synthesis of derivatives of 3,4-benzopyrene through phenalone-9 (XII).

Koelsch and Anthes [6] demonstrated that the reaction of organo-magnesium compounds with phenalone-9 leads to 1-substituted phenalones-9, through the intermediate formation of a dihydro derivative.

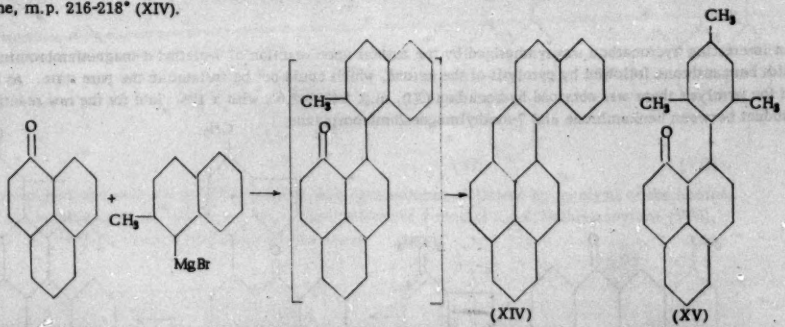
Reaction of o-magnesiumbromotoluene with phenalone-9, with subsequent pyrolysis of the ketone formed, should lead to 3,4-benzopyrene.



(XIII)

Tests conducted by the authors have shown that, upon reaction of o-magnesiumbromotoluene with phenalone-9, there is obtained, with a yield 49% of the theoretical, the ketone (XIII) (1-o-tolyl-9-phenalone), with a m.p. of 156-157°, which, upon pyrolysis, gives 3,4-benzopyrene. However, the pyrolysis gives an insignificant yield of pure 3,4-benzopyrene.

In analogous fashion, upon reaction of α-magnesiumbrom-β-methylnaphthalene with phenalone-9, with subsequent pyrolysis of the ketone, isolation of which was not accomplished, there was obtained 1', 2', 3,4-naphthopyrene, m.p. 216-218° (XIV).



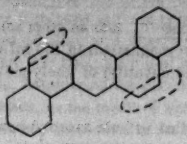
(XIV) (XV)

Reaction of magnesiumbromomesitylene with phenalone-9 leads to the formation of ketone (1-mesitylphenalone-9) (XV) in 66% of the theoretical yield, m.p. 169-171°. Its pyrolysis, however, gave a negligible amount of a compound with m.p. 213-215°, which we have not yet carefully analyzed

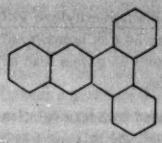
High carcinogenicity of the 3,4,6,7-dibenzopyrene synthesized by A. E. Arbuzov and N. P. Grechkin is found to be in contradiction with the declared opinion of Pullman [7] concerning the connection between carcinogenic activity and an increased electronic density in a certain orbital region of the molecule of a carcinogenic substance, corresponding to the 9,10-position of the phenanthrene skeleton in the "K" orbit.

The activity of 1,2,5,6-dibenzanthracene, according to Pullman, is connected with the presence of the "K"

orbit in the molecule (XVI). Substitution in the "K" orbital region of 1,2,3,4-dibenzanthracene (XVII) leads to loss of the carcinogenic activity.



(XVI)



(XVII)

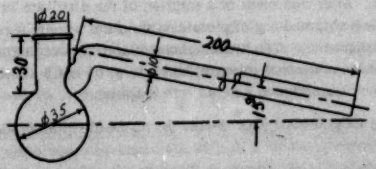
3,4,6,7-Dibenzopyrene and its derivatives could be regarded as derivatives of 1,2-benzanthracene, in which the "K" orbit is substituted. At the same time the hydrocarbon obtained was found to be highly carcinogenic. It is true that there is another "K" orbit region that has preserved the 9,10-position of the phenanthrene nucleus, but it obviously comes closer to the chrysenic grouping, inactive in the sense of carcinogenicity.

On the other hand, 2', 3'-naphtho-3,4-pyrene, where the "K" and "K_1" orbital regions are free, were found to be non-carcinogenic, as was indicated at the beginning of the present article.

EXPERIMENTAL

Reaction of 7-methyl-4-magnesiumbromindane with 1,9-benzanthrone-10. To 1.7 g of magnesium in 50 ml of ether was added a few drops of ethyl bromide; after reaction was started, there was added to the flask 15 g of 4-bromo-7-methylindane [8]. The reaction mass was boiled for 18 hours during that time the greater portion of the magnesium dissolved. Into the cooled mixture, at room temperature, was sprinkled 8 g (half the calculated quantity) of finely-ground benzanthrone (m.p. 169-170°). Upon adding the benzanthrone, local boiling of the ether resulted. After all of the benzanthrone had been added, the mixture was boiled for 3 hours; the ether was subsequently driven off and replaced by benzene; and the mixture was again heated to boiling for 5 hours. After cooling, followed by decomposition with water and dilute acetic acid, the benzolic layer was separated and subjected to steam distillation; residue – 8 g of orange-colored tar resembling sealing wax. During unsuccessful attempts, to crystallize the obtained product, there was isolated 1.5 g of unreacted benzanthrone. The remainder was dried in vacuo to the solid state and this form was subjected to pyrolysis.

Pyrolysis of the product obtained by reaction of 4-magnesiumbromo-7-methylindane with 1,9-benzanthrone-10. 6.2 g of the substance was divided into 4 equal portions, which were individually subjected to pyrolysis. Each 1.5 g of initial product was placed in a small flask of heat-resisting glass, with a low, wide outlet fused into the base of the neck; the dimensions of the flask are visible in the attached drawing.



Pyrolysis was conducted in a bath of Wood's alloy at 380-410° for 30-40 minutes. After evolution of water ceased, the pyrolysis products were distilled in vacuo at 2-3 mm, the bath temperature during distillation being 420-460°. 0.5 g of hard transparent distillate was obtained.

The remaining initial substance was reprocessed under the same conditions. In all there was obtained 1.8 g of hard distillate. After a series of recrystallizations from benzene there was obtained 0.68 g of pure crystalline substance in the form of thin yellow needles, m.p. 241-242.5°. Yield was 7.0% of the theoretical,

on the basis of benzanthrone reacted.

0.0936 g substance: 0.3247 g CO_2; 0.0460 g H_2O. Found %: C 94.58; H 5.46. $C_{27}H_{18}$. Calculated %: C 94.78; H 5.27.

Reaction of magnesiumbromomesitylene with 1,9-benzanthrone-10. Into an ether solution of magnesiumbromomesitylene, prepared from 50 g of bromomesitylene and 6 g of magnesium in 150 ml of dry ether, there was sprinkled at room temperature 25 g (less than half the calculated quantity) of finely-pulverized benzanthrone. Time of addition was 40 minutes.

Reaction was accompanied by heat evolution. The ether boiled without external heating. When all of the benzanthrone had been added, the mixture was boiled for 1 hour. After decomposition of the cooled mixture with ice and dilute acetic acid, crystals precipitated immediately, which were filtered off. After separation of the ether layer and driving off of the ether, there was obtained an additional quantity of crystals. The total of crude substance was 33 g. After its recrystallization from benzene, there was obtained 22.3 g of yellow crystals, m.p. 167-168.5°. Yield 59% of theoretical, on the basis of benzanthrone.

0.1115 g substance: 0.3657 g CO_2; 0.0584 g H_2O. Found %: C 89.47; H 5.82. $C_{36}H_{26}O$. Calculated %: C 89.60; H 5.80.

Pyrolysis of 4-mesityl-1,9-benzanthrone-10. 14 g of mesitylbenzanthrone was subjected to pyrolysis in five approximately equal portions. Pyrolysis was conducted at a temperature of 380-410° for 30-40 minutes. The pyrolysis products were subjected to distillation under a vacuum of 2-3 mm, the bath temperature during distillation being 410-430°. The total obtained was 6 g of hard transparent distillate. After a series of recrystallizations from benzene, there was obtained 0.92 g of light yellow crystals, in the form of small needles. M.p. 166-167.5°. Yield 10.2%, based on mesitylbenzanthrone. Picrate from alcohol, m.p. 194-196°.

Analysis of the substance with m.p. 166-167.5°.

0.1204 g substance: 0.4173 g CO_2; 0.0601 g H_2O. Found %: C 94.52; H 5.55. $C_{36}H_{18}$. Calculated %: C 94.52; H 5.48.

Reaction of 2-mangesiumbromoparacymene with 1,9-benzanthrone-10. To the ether solution of 2-magnesiumbromoparacymene, obtained from 50 g o-bromoparacymene and 5.5 g of magnesium in 150 ml of dry ether, was added, portionwise over 30 minutes, 20 g of finely-powdered benzanthrone (40% of the calculated weight). The ether boiled at the expense of the heat evolved during the reaction. The reaction mass was boiled on a water bath for 1 hour, and after 1 hour was decomposed with water and dilute acetic acid. The ether layer was separated and distilled. After the previous distillations of ether with steam, there was obtained 31 g of orange-colored tar residue resembling sealing wax, soluble in many of the organic solvents, but non-crystallizable from any of them.

Pyrolysis of 4-(paracymene)-1,9-benzanthrone-10. 18 g of resinous product, obtained by the reaction of magnesiumbromoparacymene with benzanthrone, was subjected to pyrolysis in six 3-gram portions. The pyrolysis was carried out in a bath of Wood's metal at a temperature of 380-410° for 20-25 minutes (cessation of water evolution). The pyrolysis products were distilled from the flask of above-designed construction at a vacuum of 2-3 mm; temperature of distillation, 360-430°. As a result of the distillation there was obtained 5.6 g of a hard, transparent substance. After treatment of a solution of the distillate in benzene with the calculated weight of picric acid, there was obtained 5 g of picrate in the form of cherry-colored needles, m.p. 165-169° (recrystallized from alcohol-benzene). The hydrocarbon isolated by decomposition of the picrate after a few recrystallizations (from benzene-alcohol mixture) had a m.p. of 124.5-126.5°. Yield was 1 g or 5.5% of theoretical, on the basis of the benzanthrone entered into reaction.

0.1053 g substance: 0.3653 g CO_2; 0.0516 H_2O. Found %: C 94.62; H 5.45. $C_{27}H_{18}$. Calculated %: C 94.17; H 5.83.

Reaction of α-magnesiumbromotetralin with 1,9-benzanthrone-10. 12 g of finely ground benzanthrone was added to a solution of magnesiumbromotetralin, obtained from 22 g of the bromide and 2.5 g of magnesium in 100 ml of dry ether. Upon addition of the benzanthrone, the ether boiled up, and the benzanthrone changed into a solution, acquiring a brown pigmentation with green fluorescence. After all of the benzanthrone had been added, there appeared a dark oil on the bottom of the flask. The flask was further heated to boiling of the solvent for 2 hrs. After decomposition with water and dilute acetic acid there was obtained a dark oil which

was subjected to steam distillation. As a result of the distillation, there was obtained 14.2 g of hard, sealing wax-like tar, which could not be crystallized. This product was directly subjected to further pyrolysis.

Pyrolysis of the product obtained by the reaction of 2-magnesiumbromotetralin with benzanthrone. 10 g of the resinous product was pyrolyzed in three portions at a temperature of 360-390° for 20-25 minutes. The product of the pyrolysis was distilled on a Wood's metal bath under a 2-3 mm vacuum; the maximum temperature in the bath was 500°. There was obtained 6 g of hard distillate, which was dehydrated with sulfur (the theoretical amount of sulfur was taken, considering the distillate as pure substance). The mass obtained after dehydration was resubjected to distillation, as the result of which there was obtained 2 g of hard distillate. After multiple recrystallizations from benzene-alcohol mixture, there was obtained 0.15 g of substance in the form of light yellow needles, with m.p. 206-207°. From the mother liquor of the last recrystallization, there was obtained also 0.06 g of the substance, with a m.p. of 205.5-207°.

0.0193 g substance: 0.0676 g CO_2; 0.0077 g H_2O. Found %: C 95.50; H 4.43. $C_{27}H_{16}$. Calculated %: C 95.28; H 4.72.

Reaction of magnesiumbromo-m-xylol with benzanthrone. To an ether solution of magnesium bromo-m-xylol, taken in excess, was added 20 g of pulverized benzanthrone. Upon addition of the benzanthrone, the ether boiled up and the solution finally heated up to boiling. After 1 hour and a half of boiling, the cooled solution was decomposed with water and dilute acetic acid. The water layer was separated and the solution subjected to steam distillation. In the residue was a sealing wax-like mass, of brown color; weight after drying was 30 g. The substance was soluble in the usual organic solvents, but did not recrystallize from any of them.

Pyrolysis of the product obtained by reaction of magnesium-m-xylol with benzanthrone. 17.9 g of the resinous product was subjected to pyrolysis at a temperature of 390-420° for 20 minutes. The product of pyrolysis was extracted with benzene. To the benzene extract was added an alcoholic solution of picric acid, calculated on the hydrocarbon content of 50% of the product taken from pyrolysis. The isolated picrate (2.5 g) failed to purify. From the products of decomposition of the picrate with ammonia, after a series of recrystallizations from benzene-methanol mixture, the isolation of a yellow-gray crystalline substance, m.p. 172-174°, was successful. Yield 0.15 g, about 1% of the theoretical, on the basis of benzanthrone.

0.0139 g substance: 0.0485 g CO_2; 0.0062 g H_2O. Found %: C 95.15; H 4.96. $C_{25}H_{16}$. Calculated %: C 94.93; H 5.07.

Reaction of o-magnesiumbromotoluene with phenalone-9. To an excess (three times the calculated weight) of o-magnesiumbromotoluene in ether solution (21.90 g of bromotoluene, 3 g magnesium and 100 ml of ether) there was added 7.7 g of phenalone-9. Upon addition of the ketone, considerable heating up occurred and the ether boiled up, the solution acquiring a dark-red color. After boiling for half an hour, the cooled solution was decomposed with ice and acetic acid.

After driving off the solvent and toluene with steam, the residue crystallized; 11.6 g of raw substance was obtained. After recrystallization from benzene and from acetic acid, there was obtained 5.7 g (or 49% of the theoretical) of a substance with a m.p. of 156-157°.

0.0905 g substance: 0.2923 g CO_2; 0.0483 g H_2O. Found %: C 88.08; H 5.92. $C_{20}H_{16}O$. Calculated %: C 88.22; H 5.88.

Pyrolysis of 1-o-tolylphenalone-9. 4 g of ketone was subjected to pyrolysis at 360-380° for 30 minutes. The pyrolysis products were distilled in vacuo (2-3 mm); temperature of distillation 370-410°. 0.6 g of crystalline distillate was obtained. After a few recrystallizations, there was obtained 0.15 g of 3,4-benzopyrene with m.p. 174-176°. Yield 4% of theoretical.

Reaction of α-magnesiumbromo-β-methylnaphthalene with phenalone-9. To the ether solution of α-magnesium-bromo-β-methylnaphthalene, obtained from 20 g of α-bromo-β-methylnaphthalene and 2 g of magnesium (both substances taken in double the quantity as regards phenalone-9) was added by portions 8.5 g of finely-ground phenalone-9. Upon addition of the ketone, the ether boiled up and the ketone turned into a solution. Time of addition was 30 minutes. The solution was further heated to boiling for 1.5 hrs. After cooling, the reaction mixture was decomposed with ice and dilute acetic acid. As the result of driving off the ether, and steam distillation of the residue, there was obtained 16.8 g of hard sealing wax-like resin, brown in color. Attempts to isolate pure β-methylnaphthylphenalone-9 were unsuccessful.

Pyrolysis of the product obtained by reaction of α-magnesium-bromo-β-methylnaphthalene with phenalone-9. 12 g of the sealing wax-like product was subjected to pyrolysis in six portions, at a temperature of 370-400° for 20 minutes. The main bulk of water was eliminated at 370-390°. Upon completion of pyrolysis, the residue in the flask was distilled in vacuo (3 mm), temperature of the distillation 390-435°; at the outlet tube of the flask the distillate partially crystallized. In all there was obtained 2.6 g of highly impure crystalline substance. After recrystallization from benzene-methanol mixture there was obtained 1.2 g of yellow crystals in the form of small flakes, with a m.p. 204-209°. After a few recrystallizations there was separated 0.8 g of crystals with a m.p. of 216-218°.

0.0931 g substance: 0.3252 g CO_2; 0.0419 g H_2O. Found %: C 95.30; H 5.02. $C_{24}H_{14}$. Calculated %: C 95.36; H 4.64.

Reaction of magnesiumbromomesitylene with phenalone-9. To an ether solution of magnesiumbromomesitylene (threefold excess), obtained from 38.8 g of bromomesitylene and 4.0 g of magnesium in 170 ml of ether, was added 10 g of phenalone-9, in powder form. There occurred quite a vigorous reaction, as a result of which the ether boiled up. After boiling for 1 hour, and decomposing the cooled mixture with water and dilute acetic acid, the total was subjected to steam distillation. As a result there was obtained a crystalline residue, contaminated by resinous substances. After a series of recrystallizations from glacial acetic acid, there was obtained 12 g of the substance with a m.p. of 160-171° (yield 66% of theoretical).

0.0780 g substance: 0.2529 g CO_2; 0.0451 g H_2O. Found %: C 88.41; H 6.43. $C_{21}H_{12}O$. Calculated %: C 88.59; H 6.04.

Pyrolysis of 1-mesitylphenalone-9. 10 g of 1-mesitylphenalone-9 was subjected to pyrolysis in five portions, at a temperature of 370-400° for 25 minutes. At the end of this time, the products of pyrolysis underwent distillation in vacuo (2-3 mm); temperature of the bath 390-420°. After multiple recrystallizations from benzene-methanol mixture, there was obtained 0.03 g of substance with m.p. 213-215°. Yield negligible.

SUMMARY

1. As the experiments of Vylegzhanin have demonstrated, 3,4,6,7-dibenzopyrene and 1',2', 3,4-naphtho-6,7-benzopyrene, previously synthesized by Arbuzov and Grechkin, have been shown to possess high blastomogenic activity, which spurred the synthesis of derivatives of 3,4,6,7-dibenzopyrene.

2. Corresponding 4-substituted-benzanthrones have been synthesized by reaction of benzanthrone with organomagnesium compounds containing the methyl or methylene group in the o-position. By pyrolysis of the latter, derivatives of 3,4,6,7-dibenzopyrene have been obtained.

Thus 3-methyl-3,4,6,7-dibenzopyrene, 1', 3'-dimethyl-3,4,6,7-dibenzopyrene, 2'-isopropyl-3,4,6,7-dibenzopyrene, 3'-methyl-4',5-ethylene-3,4,6,7-dibenzopyrene and 3,4,6,7-tribenzopyrene have been synthesized.

3. In similar fashion, starting with phenalone-9 through 1-substituted phenalones by pyrolysis, were synthesized 3,4-benzopyrene, and 1',2',3,4-naphthopyrene (not described in the literature).

4. The high carcinogenic activity of 3,4,6,7-dibenzopyrene and the inactivity of 2',3'-naphtho-3,4-pyrene contradict the opinions of Pullman concerning the connection between carcinogenicity and the presence of a specific "K" orbit region in the molecule of the carcinogenic substance, with an increased density of π-electrons.

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CYCLIZATION IN THE HALOUREIDE SERIES

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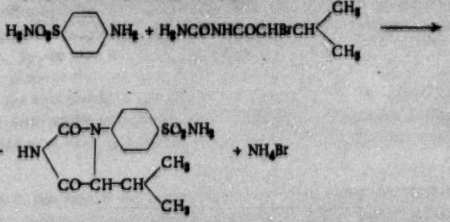
It has been pointed out that para-sulfamidophenylglycine (sulfaglycine) is considerably more effective against hemolytic streptococci than is sulfanilamide [1,2]. Its curative action on pneumonia has been demonstrated. The author has set as his goal the isolation of homologs of "sulfaglycine". By interaction of α-bromopropionic acid with sulfanilamide, in the presence of sodium hydroxide and sodium acetate, the corresponding compound is obtained with comparative ease; the yield, however, is small, because this substance is characterized by high solubility in water.

The method indicated above is not applicable to the isolation of the analogous compound from sulfanilamide and α-bromoisovaleric acid. All attempts to obtain this compound by the usual methods were unsuccessful. The author decided to fuse together sulfanilamide (m.p. 164°) with the ureide of α-bromoisovaleric acid (bromoural). The ureide of "sulfavaline" was of considerable interest in itself; from it can be obtained, without difficulty, "sulfavaline" itself.

The mixture of sulfanilamide with bromoural (m.p. 150°) melts at 130-135°. After about 45 minutes, the mass begins to thicken; within 2-2.5 hours it becomes completely hard, which demonstrates that the melting point of the product formed exceedsconsiderably the melting points of the ingredients. It should be noted that condensation is accompanied by considerable heat evolution.

If the process were to proceed in a normal fashion, the nitrogen content of the condensation product would be 17.83%. Analysis shows that the compound produced contains 14.32% nitrogen, which is 20% lower than that calculated on the assumption of a normal condensation. Because, on a percentage basis, the greatest nitrogen content is in the ureide part of the molecule, and thus the most vulnerable part, the hydrogen loss should be sought for here. Solution of the melt in sodium hydroxide was accompanied by considerable ammonia evolution. These circumstances prompted us to propose the following reaction:



This combination corresponds exactly with the percent nitrogen, carbon and hydrogen found.

The compound obtained could be regarded as hydantoin, where the N-hydrogen (in position 1) is substituted by sulfamidobenzene, and the C-hydrogen (in position 5) is substituted by the isopropyl radical.

From sulfanilamide and adaline (the ureide of bromodiethylacetic acid) an analogous product was obtained.

EXPERIMENTAL

8.5 g (1/20 mole) of sulfanilamide and 11 g (1/20 mole) of bromoural were melted together in a round-bottomed flask of 50-100 ml capacity, placed in an oil bath. At 130-135° the mixture melted. After approximately 45 minutes, the mixture began to thicken, and the temperature slowly rose to 150-155° in the mass (bath temperature 135-140°). Within 2.5 hours the reaction mass was completely hard, and reaction was complete. The melt was dissolved in a 3% solution of sodium hydroxide. When all of the melt was dissolved, activated carbon was added; the mixture was stirred for about a half-hour at 40-50°. The solution was then filtered and supersaturated with 10% hydrochloric acid. The precipitate was filtered off, washed with water to free it from

the hydrochloric acid and from the mineral salts, and dried. The dried product was extracted 2-3 times with hot chloroform. The precipitate filtered from the chloroform was boiled in a mixture of methanol (300 ml) and water (150 ml) in the presence of activated carbon. After 1/2 hour it was filtered off; from the filtrate upon cooling, there precipitated large white crystals, M.p. 256°. Yield of crude product ~9 g. Yield of pure sample was 7.5 g (the mother liquor was not utilized).

3.358 mg substance: 5.954 mg CO_2; 1.655 mg H_2O. 7.035 mg substance: 7.19 ml N_2. Found %: C 48.36; H 5.52; N 14.32. $C_{12}H_{12}O_4N_2S$. Calculated %: C 48.48; H 5.15; N 14.14.

SUMMARY

A new compound $C_{12}H_{12}O_4N_2S$ was obtained by melting together sulfanilamide and bromoural, which the author regards as a 1,5-disubstituted derivative of hydantoin.

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ACONITE ALKALOIDS

V. ELDELINE AND ELDELIDINE

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The high toxicity of the various aconites of larkspur, a variety of plants rich in alkaloids, long ago attracted the attention of both Soviet and foreign investigators. During the past ten years there have been published about 10 Soviet and 20 foreign works, devoted to the study of this group of alkaloids, which is distinguished by marked physiological activity and extraordinary complexity of chemical structure.

Soviet investigators have already isolated upwards of twelve alkaloids from different varieties of larkspur and the aconites which grow in Soviet Union territory, and a relationship between them has been determined which enables all of the works on them to be incorporated into one group under the joint title of "The Aconite Alkaloids" [1]. The works of Konovalova and Orekhov [2] have also established a most interesting regularity, as follows: if one mentally substitutes all of the replaceable groups (hydroxyl, methoxyl, N-alkyl, and others) in the formulas of the aconite alkaloids by hydrogen, it will be seen that all lead to one and the same formula, $C_{19}H_{29}N$. In the following Soviet works – Rabinovich and Konovalova [3], Yunusov and Abubakirov [4], assumption was further made concerning the possibility of grouping the formulas of some of the aconite alkaloids under the general formula, $C_{20}H_{31}N$.

In Table 1 are listed alkaloids isolated by Soviet chemists over the past ten years.

The data quoted in the table unquestionably confirm Orekhov and Konovalova's assumption that the heterocyclic nucleus, $C_{19}H_{29}N$, or $C_{20}H_{31}N$, is common to all of the aconite alkaloids.

In the present article are reported the results of investigations of one variety of larkspur - Candle larkspur (Delphinium elatum). The variety indicated has been repeatedly investigated by various foreign workers. In the first work, published by Keller in 1925, there was reported the derivation of alkaloids from the seeds of this plant, in amounts approximating 1% of the seed weight, and the isolation of a crystalline alkaloid with a m.p. of 218°, of composition $C_{33}H_{53}O_8N$. In addition, Goodson [9] published an article in 1943, wherein he reported alkaloids from the seed of the same plant to the sum of 1.7%, from which the author isolated three crystalline alkaloids: delpheline, m.p. 227°, of the composition $C_{22}H_{33}O_8N$, delatine, m.p. 148°, of the composition $C_{19}H_{25}O_3N$, and methyllycaconitine in the form of the hydriodide, m.p. 201°, of the composition $C_{37}H_{48}O_{10}N_2 \cdot HI \cdot 2H_2O$. In 1944 the same author published a work [10] in which a different composition was ascribed to delpheline, namely $C_{25}H_{39}O_6N$.

Upon investigation of the variety of larkspur in question, the author has obtained results which differ from those published previously. Such a difference should be explained first of all by the fact that the authors mentioned studied the alkaloids obtained from the seeds, whereas this author studied the stems and the leaves. Secondly, geographical and climatic conditions are entirely different in the locality where the investigated specimens grow.

The candle larkspur specimen investigated by the author was collected by an expedition from the All Union Chemico-Pharmaceutical Institute of Scientific Research, under the direction of P. S. Massagetov during the period of the end of July and beginning of August, at blossoming time, along the banks of the river Ulba (in the Altai region).

All of that part of the plant which grows above ground was extracted with alcohol. The sum of the alkaloids isolated amounted to 0.25% of the plant dry weight. It should be noted that the alkaloid content of the leaves is considerably higher than that of the stems: thus, when the sum of the alkaloids in the leaves attains 0.85%, the stalks contain only 0.15% of the dry weight of initial raw material. Upon concentration of the ether extract, there immediately crystallized out an alkaloid, which, after purification in the form of its salt, melted at 182-184°, and exhibited a specific rotation of 32.46°. The alkaloid forms readily-crystallizable salts: hydrochloride, hydriodide, perchlorate, oxalate, nitrate. On the basis of an elementary analysis, both of the base and of its salts, it was possible to determine its composition $C_{27}H_{41}O_8N$.

TABLE 1

No.	Alkaloid	Composition	Partly-developed formula	Basic nucleus	Author
1	Thalatisamine	$C_{22}H_{35}O_4N$	$C_{19}H_{24}(NH)(OH)(OCH_3)_3$	$C_{19}H_{29}N$	Konovalova, Orekhov [2]
2	Thalatisidine	$C_{23}H_{37}O_5N$	$C_{19}H_{25}(NC_2H_5)(OH)_3(OCH_3)_2$	$C_{19}H_{29}N$	
3	Isothalatisidine	$C_{23}H_{37}O_5N$	$C_{19}H_{25}(NC_2H_5)(OH)_3(OCH_3)_2$	$C_{19}H_{29}N$	
4	Thalatisine	$C_{20}H_{29}O_3N$	$C_{19}H_{23}(NCH_3)(OH)_3$	$C_{19}H_{29}N$	
5	Delphamine	$C_{25}H_{41}O_7N$	$C_{19}H_{25}(NC_2H_5)(OH)_4(OCH_3)_3$	$C_{19}H_{31}N$	Konovalova and Rabinovich [3] The same [1]
6	Condelphine	$C_{25}H_{39}O_8N$	$C_{19}H_{25}(NC_2H_5)(OH)_2(OCOCH_3)(OCH_3)_2$	$C_{19}H_{29}N$	
7	Songorine	$C_{21}H_{29}O_3N$	$C_{19}H_{23}(NC_2H_5)(OH)_2(CO)$	$C_{19}H_{29}N$	Yunusov [5]
8	Delphatine	$C_{26}H_{43}O_7N$	$C_{19}H_{21}(NC_2H_5)(OH)_2(OCH_3)_5$	$C_{19}H_{29}N$	Abubakirov [6]
9	Delbine	$C_{33}H_{55}O_{10}N_3$	$C_{19}H_{21}(NC_2H_5)(OH)(OCH_3)_5(OCOC_6H_4NHCOCH(CH_3)CH_2CONH_2)$	$C_{19}H_{29}N$	
10	Delsamine	$C_{37}H_{53}O_{10}N_3$	$C_{19}H_{21}(NC_2H_5)(OH)_2(OCH_3)_4(OCOC_6H_4NHCOCH(CH_3)CH_2CONH_2)$	$C_{19}H_{29}N$	
11	Delsine	$C_{25}H_{41}O_7N$	$C_{19}H_{21}(NC_2H_5)(OH)_3(OCH_3)_4$	$C_{19}H_{29}N$	
12	Amino alcohol of delartine	$C_{26}H_{43}O_7N$	$C_{20}H_{25}(NC_2H_5)(OH)_3(OCH_3)_4$	$C_{20}H_{31}N$	Rabinovich and Konovalova [7]

The alkaloid isolated by the author contains three methoxyl, one hydroxyl and an N-alkyl group. The methoxyl and the N-alkyl groups were determined by the method of Fibock. The presence of the hydroxyl group was demonstrated by the formation of a monoacetyl derivative. It is of interest to note that the authors succeeded in acetylating the base only upon prolonged heating of the alkaloid with acetyl chloride in a sealed tube, similar to that of isothalatisidine [4], delphamine [5] and the amino-alcohol of delartin [6]. A new substance, of the composition $C_{29}H_{45}O_9N$, was obtained as the result. Upon heating with acetic anhydride in pyridine medium the unchanged base was recovered. Our alkaloid exhibits unusual behavior relative to methyl iodide, resembling in this respect the amino alcohol of delartine [6] and dekine [7]. As with the cases indicated, during this reaction the hydriodide of the initial alkaloid is formed, rather than the expected methyl iodide, exactly identical with the product which results when the alkaloid and hydriodic acid are interacted.

It should be observed that among the aconite bases described in the literature, is the known alkaloid, deltaline [11], isolated in 1936 from Delphinium occidentale. Deltaline, in its melting point, specific rotation and elementary analysis data, resembles very much the alkaloid isolated by the author from Candle larkspur. However, its resemblance is limited to these constants only; thus, according to the literature data, attempts to isolate any crystalline salts of deltaline were unsuccessful, whereas a pure alkaloid will form well-defined salts with both inorganic and organic acids. There was described only an auric salt of deltaline, which melted at 120-125°, whereas the chloraurate of our alkaloid melts at 175°. In agreement with the analytical data, deltaline was said to contain two methoxyl groups, and respectively was described its triacetyl derivative with m.p. 270-272°. The alkaloid isolated by the author contains three methoxyl groups and one hydroxyl group. The monoacetyl derivative obtained melts at 142-144°. Comparative data are quoted in Table 2.

Thus, the author has reason to believe that this is a new alkaloid which has not been described in the literature. The alkaloid has been named "eldeline" by the author.

Considerable difficulty was encountered in separating the alkaloid mixture obtained from the mother liquor after separation of eldeline. Attempts to apply the method of fractional separation based upon basicity, to obtain crystalline salts, and to utilize the methods of chromatography were all unsuccessful. The author finally

TABLE 2

Constants	Deltaline [11]	Base from Candle larkspur
Melting point and $[\alpha]_D$	180-181°; −27.86°	182-184°; −32.4°
Carbon content (%)	63.37, 63.71	64.10, 63.82
Methoxyl group content (%)	15.68	18.27
Functional group	$(OCH_3)_3(OH)_3$	$(OCH_3)_3OH$
Melting point of chloraurate	120-125°	170-175°
Melting point of acetyl derivative	270-272°	142-144°

succeeded in isolating another crystalline alkaloid only by discovering an interesting property – the solubility of its sulfate in chloroform. Base No. 2, thus isolated, is much more difficultly soluble in organic solvents than is eldeline. After recrystallization from alcohol, the alkaloid, not yet carefully studied, melted at 212-214°. After removal of eldeline and base No. 2, there still remains about 0.1% of a non-crystallizable mixture of alkaloids, procedures for the separation of which are still under investigation.

Eldeline was found to be an ester, which saponified upon heating the base in a water-alcohol solution of alkali. Accordingly, a crystalline amino alcohol was isolated, crystallizing well from alcohol, with a m.p. of 226-228°, and with a specific rotation of −17.08°. The amino alcohol obtained by the author forms well-defined salts: hydrochloride, hydriodide, nitrate and oxalate. According to the elementary analysis data, both of the base and of its salts, the composition of the amino alcohol was determined to be $C_{25}H_{39}O_7N$. As can be seen from the empirical formula of eldeline $C_{27}H_{41}O_8N$, and its amino alcohol $C_{25}H_{39}O_7N$, the first is found to be the acetate ester of the second.

Determination of functional groups in the amino alcohol has demonstrated the presence of three methoxyl, two hydroxyl and one N-alkyl group. The nature of the two remaining oxygen atoms was clarified by determination of the presence, in the amino alcohol, of the methylenedihydroxy group, proven by the known qualitative reaction obtained upon heating with phloroglucinol. The character of the N-alkyl group was ascertained by oxidation of the amino alcohol. Upon reaction of an acid solution of potassium permanganate, followed by cooling, there occurred a splitting off of the N-alkyl group to form an aldehyde, as was proven to be the case with delphamine [3], condelphine [1] and other alkaloids of the aconite group. With an N-methyl group there is formed formaldehyde; in the presence of an N-ethyl group there is formed acetaldehyde. Upon oxidation of the amino alcohol of eldeline, formaldehyde separated, which was identified by its condensation product with dimedone.

In this manner, the partially-developed formulas for eldeline and for its amino-alcohol are found to be as follows:

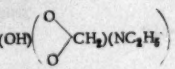
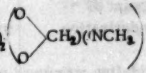
Eldeline $C_{27}H_{41}O_8N$ $C_{20}H_{23}$ { $(OCH_3)_3$, (OH), $(OCOCH_3)$, O_2CH_2, (NCH_3) }

Amino alcohol of eldeline $C_{25}H_{39}O_7N$ $C_{20}H_{23}$ { $(OCH_3)_3$, $(OH)_2$, O_2CH_2, (NCH_3) }

and of course the framework of these two new aconite alkaloids is their characteristic heterocyclic ring.

The amino alcohol behaves like eldeline in its reaction with methyl iodide; instead of the expected methyl iodide (addition complex), the hydriodide of the original base is formed. A study of the acetylation of the amino alcohol yielded interesting results: there was formed the monoacetyl derivative of the alcohol, found to be identical with eldeline, when the former was reacted with acetic anhydride in pyridine. Reaction with acetyl chloride yielded the diacetyl derivative, found to be identical with the monoacetyl derivative of eldeline. Saponification of the latter with a water-alcohol solution of alkali yielded the unchanged amino alcohol. In

TABLE 3

	Delpheline [9,10]	Amino alcohol of eldeline
Base	M.p. 227° $[\alpha]_D = -25.8°$	M.p. 226-228° $[\alpha]_D = -17.08°$
Hydrochloride	M.p. 219° $[\alpha]_D = -42.8°$	M.p. 214-216° $[\alpha]_D = -31.3°$
Nitrate	M.p. 191-193° $[\alpha]_D = -41.2°$	M.p. 186-188° $[\alpha]_D = -41.4°$
Base content	$C_{25}H_{39}O_6N$ [10]	$C_{25}H_{39}O_7N$
Functional groups	$(OCH_3)_3(OH)$ 	$(OCH_3)_3(OH)_2$ 
Monoacetyl derivative	M.p. 125° $[\alpha]_D = -34.5°$	182-184° $[\alpha]_D = -32.46°$
Diacetyl derivative	—	M.p. 142-144° $[\alpha]_D = -25.4°$

this way, by saponification and by acetylation, the author has succeeded in proving that eldeline is the acetate ester of the amino alcohol.

The author has shown above that the bases isolated from the given specimen of Delphinium elatum differ from the alkaloids described in the literature; however, the product of saponification obtained by the author – the amino alcohol of eldeline – resembles in its properties the alkaloid delphine, isolated by Goodson [9] in 1943 from the plant species named. The isolation of two bases from one and the same plant species makes their identity quite possible. However, a more thorough investigation of the amino-alcohol of eldeline proved that these substances are different. In Table 3 the properties of the two bases are compared.

As can be seen from the data quoted, these bases differ in their composition, in the number of hydroxyl groups, the character of the N-alkyl group, and in the properties of the acetyl derivatives. Thus, the amino alcohol of eldeline is found to be a new substance, not described in the literature, which gives the author the privilege of naming it "eldelidine".

All of the analytical determinations were conducted in the microanalysis laboratory under the supervision of candidate of chemical science V. V. Kolpakova. The author is very much indebted to her for these determinations.

EXPERIMENTAL

1. Isolation and Separation of the Alkaloids. 10 g of the pulverized plant was extracted with isopropyl alcohol, containing 1% of acetic acid. The alcohol extract was steamed in vacuo at a water bath temperature not exceeding 40-50°. The thick resinous substance obtained was dissolved in 10% sulfuric acid, and the acid solution was treated with benzene to remove the resin. The considerably clarified sulfate solution, after cooling with ice, was made alkaline with 25% ammonia, after which exhaustive extraction with diethyl ether was made. After the ether extract had been dried with anhydrous sodium sulfate, the ether was distilled off to a volume of 100-120 ml. After cooling the concentrated solution, a base crystallized out, named "eldeline", in the form of light-colored needle crystals, which were vacuum filtered, washed with diethyl ether and dried in a vacuum dessicator. 11 g of crude eldeline was isolated, m.p. 176-180°. The mother liquor, after separation of the eldeline, was treated with 10% sulfuric acid. The sulfate solution so obtained was extracted with approximately five times the volume of chloroform.

a) Treatment of the chloroform solution. The chloroform was distilled off in vacuo, and the remaining syrupy substance was dissolved in a few ml of 10% sulfuric acid, and the acid solution was washed several times with ether, and then made alkaline with 25% ammonia, and then exhaustively extracted with ether. After steaming off the latter, there crystallized out about 1 g of Base No. 2, with a m.p. of 204-208°. After recrystallization from 10 times its volume of 96% alcohol, the base melted at 212-214°.

b) Treatment of the sulfate solution. The acid aqueous solution remaining after the chloroform extraction was made alkaline with 25% ammonia and then exhaustively extracted with ether. After concentration of the ether solution, an additional 2 g of eldeline crystallized out, and there remained about 10-11 g of a non-crystallizing alkaloid mixture, which has not as yet been investigated.

In all, there were isolated, from 10 kilograms of raw material, 13 g of eldeline, 1 g of Base No. 2 and 10-11 g of non-crystallizable bases. The sum total of the alkaloids thus consisted of 25 g, or 0.25% of the dry weight of the above-ground portions of the plant.

Upon separation of the alkaloids by the described method, there were obtained, separately, from the leaves and from the stems, the following results. From 1 kg of leaves there were isolated 4 g of eldeline and 4.3 g of non-crystallizable bases. The total sum of alkaloids was 8.3 g, or 0.83% of the dry weight of leaves. From 1 kg of stems there was isolated 0.5 g of eldeline and 1 g of non-crystallizable bases. The total sum of alkaloids was 1.5 g or 0.15% of the dry weight of stems.

2. Eldeline. The technical base, m.p. 176-180°, was purified by subsequent transformation into the hydrochloride and into the oxalate. The base, isolated from an aqueous solution of salt by the action of ammonia, was extracted with ether and recrystallized by concentration of the latter. After recrystallization from diethyl ether (1:50), it melted at 182-184°. Eldeline is difficult to dissolve in water, petroleum ether and diethyl ether; more soluble in ethyl acetate, and readily soluble in acetone, alcohol and chloroform.

0.1642 g substance: 3.25 ml alcohol; $l = 0.5$; $\alpha = -0.82°$; $[\alpha]_D = -32.46°$. 3.271 mg substance: 7.688 mg CO_2; 2.374 mg H_2O. 4.320 mg substance: 10.109 mg CO_2; 3.112 mg H_2O. 8.395 mg substance: 0.235 ml N_2 (22.0°, 728 mm). 7.145 mg substance: 0.183 ml N_2 (27.5°, 727 mm). 8.910 mg substance: 0.60 ml CH_4 (18°, 740 mm). 8.584 mg substance: 0.60 ml CH_4 (25°, 750 mm). 5.433 mg substance: 9.60 ml 0.02 N $Na_2S_2O_3$. 0.0932 g substance: 1.85 ml 0.1 N HCl (methyl red). Found %: C 64.10, 63.82; H 8.12, 8.06; N 3.10, 2.78; (OCH_3) 18.27; M 503.8. $C_{27}H_{41}O_8N$. Calculated %: C 63.91; H 8.08; N 2.76; $3(OCH_3)$ 18.34; M 507.

3. Eldeline Salts. Hydrochloride. Eldeline was mixed with an equal volume of absolute alcohol, and upon addition of alcoholic hydrochloric acid, up to the point of a slightly acid reaction to Congo red, it all went into solution. Upon gradual addition of five times the volume of absolute ether, the hydrochloride crystallized out. After recrystallization from 10 times the volume of an acetone-absolute alcohol mixture (10:1), the hydrochloride melted at 204-206° (with decomposition).

0.1120 g substance: 3 ml water; $l = 0.5$; $\alpha = -0.95°$; $[\alpha]_D = -50.89°$.

5.000 mg substance: 1.415 mg AgCl. 5.494 mg substance: 1.554 mg AgCl. Found %: Cl 7.00, 7.00. $C_{27}H_{41}O_8N \cdot HCl$. Calculated %: Cl 6.53.

Nitrate. It was obtained by mixing an acetone solution of eldeline with nitric acid, and precipitating it from the obtained solution by the use of absolute ether. It was recrystallized from absolute alcohol (1:10), crystallizing out upon addition of absolute ether; m.p. 170-173° (with decomposition).

0.0750 g substance: 3 ml water; $l = 0.5$; $\alpha = -0.6°$; $[\alpha]_D = -48°$.

5.478 mg substance: 11.450 mg CO_2; 3.649 mg H_2O. 3.314 mg substance: 6.927 mg CO_2; 2.147 mg H_2O. 7.180 mg substance: 0.331 ml N_2 (21°, 732.5 mm). 8.00 mg substance: 0.372 ml N_2 (21.5°, 732 mm). Found %: C 57.00, 57.00; H 7.45, 7.24; N 5.16, 5.20. $C_{27}H_{41}O_8N \cdot HNO_3$. Calculated %: C 56.84; H 7.36; N 4.91.

Perchlorate. It was obtained by adding a saturated aqueous solution of sodium perchlorate to a solution of eldeline in 5% hydrochloric acid. After recrystallization from absolute alcohol (1:20), it melted at 216-217° (with decomposition).

Hydriodide. It was obtained by mixing an acetone solution of the base with hydriodic acid, and it separated out upon addition of dry ether. It was recrystallized from acetone (1:30), from which it crystallized out upon addition of dry ether; m.p. 219-220° (with decomposition).

5.817 mg substance: 5.39 ml 0.01 N $Na_2S_2O_3$. 6.401 mg substance: 5.89 ml 0.01 N $Na_2S_2O_3$. Found %: I 19.60, 19.47. $C_{27}H_{41}O_8N \cdot HI$. Calculated %: I 20.0.

Oxalate. It was obtained by mixing equimolecular quantities of eldeline and of oxalic acid dissolved in acetone. It was recrystallized from 10 times the volume of acetone mixed with absolute alcohol (3:1), m.p. 190-191° (with decomposition).

0.0816 g substance: 3.1 ml alcohol; $l = 0.5$; $\alpha = -0.55$; $[\alpha]_D = -41.7°$. 3.531 mg substance: 7.519 mg CO_2; 2.252 mg H_2O. 7.486 mg substance: 12.47 ml 0.02 N $Na_2S_2O_3$. 4.941 mg substance: 7.44 ml

0.02 N $Na_2S_2O_3$. Found %: C 58.07; H 7.13; (OCH_3) 15.40, 15.56. $C_{27}H_{41}O_3N$. $C_2H_5O_4$. Calculated %: C 58.29; H 7.2; 3(OCH_3) 15.58.

Chloraurate. It was obtained by the addition of auric chloride to a solution of the base in 5% hydrochloric acid. It separated in the form of an amorphous flocculent precipitate, readily soluble in alcohol. Upon addition of a few drops of water to the alcoholic solution, the chloraurate separated in the form of a fine crystalline precipitate with m.p. 170-175°. It failed to recrystallize.

4. Methyl Iodide Reaction. 1 g of eldeline was dissolved in 3 ml of methyl alcohol, and after cooling 1 ml of methyl iodide was added. The solution was heated in a sealed tube at 70-75° for 3 hours. After cooling, the tube contents were evaporated to dryness, and the residue repeatedly treated with boiling ether to ensure complete removal of all traces of the initial eldeline. The residue, in the amount of 0.5 g, was recrystallized from 20 ml of acetone. Upon addition of dry ether, there crystallized from the filtrate the substance with a m.p. of 220-221° (with decomposition). The sample, when mixed with the hydriodide of eldeline, did not produce depression of the melting point. The base obtained by pouring into an aqueous solution of ammonia did not give a depression with eldeline.

5. Acetylation of Eldeline. 1) To 0.25 g of eldeline was added 2 ml of dry pyridine and 2 ml of acetic anhydride – within a few minutes everything was dissolved. The reaction mixture was heated at 50-60° for 15 hours, after which the pyridine and the excess acetic anhydride were driven off in vacuo. The residue was dissolved in 2-3 ml of 10% sulfuric acid, and upon cooling was acidified with 10% ammonia solution – the separated base was recrystallized from ether, and thereupon melted at 180-182°. The sample mixed with eldeline did not produce depression.

2) To 0.5 g of eldeline was added 15 ml of acetyl chloride – the resulting mixture was heated in a sealed tube at 35-40° for 35 hours, as the result of which everything dissolved. After removal of the excess acetyl chloride, the residue was dissolved in a few ml of water, and upon cooling, the solution was acidified with 10% ammonia. The isolated base was readily soluble in a majority of the organic solvents. It was possible to recrystallize it from only 5 times the volume of hexane, after which the base melted at 142-144°.

0.1208 g substance: 3 ml alcohol; $l = 0.5$; $\alpha = -0.51°$; $[\alpha]_D = -25.4°$.

6.158 mg substance: 11.915 mg CO_2; 3.429 mg H_2O. 3.740 mg substance: 8.645 mg CO_2; 2.556 mg H_2O. 8.510 mg substance: 0.204 ml N_2(24.5°, 730 mm). 8.430 mg substance: 0.206 ml N_2 (25°, 727 mm). 7.486 mg substance: 12.37 ml 0.02 N $Na_2S_2O_3$. 6.806 mg substance: 11.12 ml 0.02 N $Na_2S_2O_3$. Found %: C 63.00, 63.04; H 7.44, 7.65; N 2.64, 2.68; OCH_3 17.08, 16.88. $C_{28}H_{43}O_3N$. Calculated %: C 63.39; H 7.83; N 2.5; 3(OCH_3) 16.9.

6. Saponification of Eldeline. 5 g of eldeline was dissolved in 25 ml of alcohol, to the solution was added 20 ml of 1 normal NaOH solution, and the reaction mixture was heated on a water bath for 3 hours, after which it was evaporated almost to dryness. The semi-crystalline mass was washed with water and dried in a vacuum dessicator. The yield of base was 4.3 g, with a m.p. of 220-224°. It was recrystallized from 6 times the volume of alcohol – a colorless, crystalline substance which melted at 226-228° (with the formation of bubbles).

The aminoalcohol obtained, named "eldelidine", was almost insoluble in water, difficult to dissolve in ether, easier to dissolve in acetone and alcohol, and very easy to dissolve in chloroform.

0.2190 g substance: 3.4 ml chloroform; $l = 0.5$; $\alpha = -0.55°$; $[\alpha]_D = -17.08°$

5.318 mg substance: 12.582 mg CO_2; 4.021 mg H_2O. 3.534 mg substance: 8.344 mg CO_2; 2.678 mg H_2O. 8.645 mg substance: 0.249 ml N_2 (22.0°, 728 mm). 8.535 mg substance: 0.250 ml N_2 (24.5°, 734 mm). 6.106 mg substance: 11.78 ml 0.02 N $Na_2S_2O_3$. 0.2294 g substance: 5 ml 0.1 N HCl methyl red. Found %: C 64.52, 64.39; H 8.46, 8.47; N 3.19, 3.24; (OCH_3) 19.94; M 458.8. $C_{25}H_{39}O_7N$. Calculated %: C 64.52; H 8.38; N 3.01; 3(OCH_3) 20.0; M 465.0.

7. Eldelidine Salts. Hydrochloride. It was obtained by mixing an alcoholic solution of eldelidine with hydrochloric acid, and it crystallized out upon addition of absolute ether. It recrystallized from absolute alcohol (1:20) upon addition of an equal volume of absolute ether to an alcoholic filtrate. It melted at 216-218° (with decomposition).

0.1104 g substance: 3.6 ml water; $l = 0.5$; $\alpha = -0.48°$; $[\alpha]_D = -31.3°$.

4.910 mg substance: 1.477 ml AgCl. Found %: Cl 7.44. $C_{25}H_{39}O_7N \cdot HCl$. Calculated %: Cl 7.08.

Nitrate. It was obtained by mixing an acetone solution of eldelidine with nitric acid. It was recrystallized from aqueous acetone, after which it melted at 186-188° (with decomposition).

0.0374 g substance: 3.5 ml water; $l = 0.5$; $\alpha = -22°$; $[\alpha]_D = -41.4°$.

4.228 mg substance: 8.864 mg CO_2; 2.991 mg H_2O. 3.411 mg substance: 7.142 mg CO_2; 2.419 mg H_2O. 8.680 mg substance: 0.400 ml N_2 (22.0°, 738 mm). 7.768 mg substance: 0.359 ml N_2 (22.0°, 738 mm). Found %: C 57.17, 57.10; H 7.92, 7.94; N 5.18, 5.19. $C_{25}H_{39}O_7N \cdot HNO_3$. Calculated %: C 57.1; H 7.6; N 5.33.

Oxalate. It was obtained by mixing acetone solutions of equimolecular weights of the eldelidine and the oxalic acid. The oxalate recrystallized from 20 times the volume of acetone-absolute alcohol mixture (5:1), after which it melted at 140-142° (with decomposition).

3.203 mg substance: 6.688 mg CO_2; 2.103 mg H_2O. 2.037 mg substance: 4.221 mg CO_2; 1.361 mg H_2O. Found %: C 56.47, 56.51; H 7.35; 7.47. $C_{25}H_{39}O_7N \cdot C_2H_2O_4 \cdot H_2O$. Calculated %: C 56.54; H 7.50.

Hydriodide. It was obtained by neutralization with hydriodic acid of an acetone solution of the eldelidine, and was separated from solution by the addition of dry ether. It recrystallized from a mixture of acetone-alcohol, after which it melted at 217-219° (with decomposition).

0.0654 g substance: 2.7 ml water; $l = 0.5$; $\alpha = -0.3°$; $[\alpha]_D = -24.7°$.

8. Methyl Iodide Reaction. 0.5 g of eldelidine was dissolved in 5 ml of methyl alcohol and 1 ml of methyl iodide was then added and the solution obtained was heated in a sealed tube at 70-75° for 6 hours. After cooling, the tube contents were poured into a beaker and the excess methyl alcohol and methyl iodide driven off. The remaining crystalline substance was treated with water. An insoluble substance, to the amount of 0.2 g, was found to be present in the original eldelidine. From the aqueous solution, upon addition of ammonia, the unchanged eldelidine was recovered.

9. Acetylation of Eldelidine. 1) 0.3 g of eldelidine was mixed with freshly distilled acetic anhydride and 2.5 ml of dry pyridine. The solution obtained was heated on a water bath at 35-40° for 8 hours, after which the acetic anhydride and pyridine excesses were distilled off in vacuo. The syrupy residue was dissolved in a few milliliters of 5% sulfuric acid, the acid solution washed with ether, and then made basic with 25% ammonia solution. The base, which immediately separated, melted at 180-182°, and the sample mixed with eldelidine did not produce depression.

2) 0.5 g of eldelidine was combined with 5 ml of acetyl chloride and heated in a sealed tube at 40-50° for 40 hours, after which everything went into solution. After cooling the solution, the acetyl chloride excess was evaporated off at room temperature and the residue dissolved in 5 ml of water. The aqueous solution (after cooling in ice) was made basic with 10% ammonia solution, in the presence of ether. The separated base immediately went into the ether (layer). After concentrating the ether extract to a small volume, 0.4 g of the substance crystallized. After recrystallization from 50% alcohol (1:4), the base melted at 142-144°. A sample mixed with acetyleldeline did not give depression of the melting point.

Hydrochloride. It was obtained by neutralization of an ether solution of acetyleldeline with an alcoholic solution of hydrochloric acid. After recrystallization from 10 times the volume of an absolute ether-acetone mixture (1:2), the hydrochloride melted at 172-174°.

5.195 mg substance: 1.360 mg AgCl. 3.919 mg substance: 1.103 mg AgCl. Found %: Cl 6.47, 6.33. $C_{29}H_{43}O_9N \cdot HCl$. Calculated %: Cl 6.06.

10. Saponification of Acetyleldeline. 0.5 g of acetyleldeline was dissolved in 5 ml of alcohol, after which was added 5 ml of 1 N NaOH solution, followed by heating for three hours on a water bath, after which the solution was evaporated. The residue was treated with water, vacuum filtered, washed with aqueous alcohol, and melted at 226-228°. A sample mixed with eldelidine did not produce depression.

11. Oxidation of Eldelidine. 1 g of eldelidine was dissolved in 10 ml of 10% sulfuric acid solution. 0.34 g of potassium permanganate in 10 ml of water was added from a dropping funnel over a period of 1 hour, with stirring and cooling, to the obtained solution. After another hour of mixing, the solution lost its color, the manganese dioxide was filtered off and the filtrate was distilled into a receiver well-cooled with ice. 50 ml of 1% warm aqueous dimedone solution was added to the distillate obtained, and within a few seconds the solution became turbid, after heating for 15-20 minutes of which, the bulky flocculent precipitate, first formed, then

changed into a crystalline substance. 0.12 g of the condensation product was vacuum filtered, and recrystallized from 4 ml of hexane, after which it melted at 183-184°. The condensation product of dimedone with formaldehyde melts at 185-186°. The mixed sample did not produce depression; it melted at 184-185°.

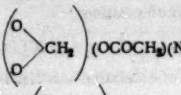
12. Determination of the dihydroxymethylene grouping. 0.02 g of eldelidine was dissolved, with heating, in 5 ml of phloroglucinol-sulfuric acid mixture. After heating on a boiling water bath, a flocculent precipitate appeared, and the solution became red, characteristic for substances with the dihydroxymethylene group.

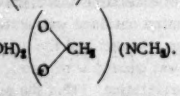
SUMMARY

1. There has been isolated a new crystalline alkaloid of the composition $C_{27}H_{43}O_8N$ from Candle larkspur (Delphinium elatum), which grows in the Altai region, which has been named "eldeline".

2. Eldeline has been found to be an ester, and upon its saponification there is formed acetic acid and a crystalline amino alcohol of the composition $C_{25}H_{41}O_7N$, named "eldelidine".

3. The partly-developed formulas of eldeline and of eldelidine have been determined:

eldeline $C_{27}H_{43}O_8N = C_{16}H_{28}(OCH_3)_2(OH)$  $(OCOCH_3)(NCH_3)$;

eldelidine $C_{25}H_{39}O_7N = C_{16}H_{28}(OCH_3)_2(OH)_2$  (NCH_3).

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